Supporting Information

Total Synthesis of (+)-Lysergic Acid

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General information

Proton NMR (^{1}H) were recorded at 400 MHz NMR spectrometer, Carbon NMR (^{13}C) at 100 MHz NMR spectrometer unless otherwise stated. The following abbreviations are used for the multiplicities: s: singlet, d: doublet, t: triplet, m: multiplet, br s: broad singlet for proton spectra. Coupling constants (*J*) are reported in Hertz (Hz).

Infrared spectra were recorded with a thin layer of the product on a KBr disk and reported in frequency of absorption (cm^{-1}).

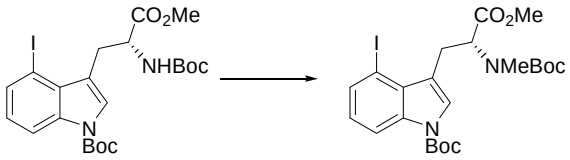
High resolution mass spectral (HRMS) data were obtained with an ionization mode of ESI.

Flash chromatography was performed using silica gel (200-300 mesh) with solvents distilled prior to use. Visualization was achieved under a UV lamp (254 nm and 365 nm), and by developing the plates with phosphomolybdic acid in ethanol.

All reagents were obtained from commercial suppliers unless otherwise stated.

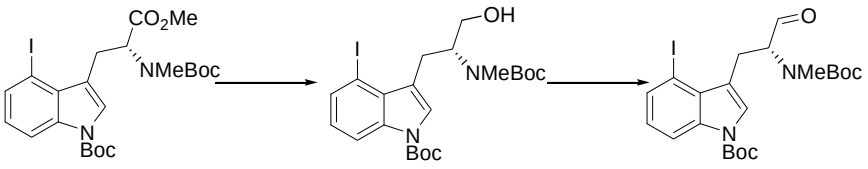
The following abbreviations are used: **FCC**: flash column chromatography; **PE**: petroleum ether; **EtOAc**: ethyl acetate; **DCM**: dichloromethane; **DMF**: *N, N*-dimethylformamide; **TMSOTf**: trimethylsilyl trifluoromethanesulfonate.

Experimental procedure and physical data



R-5 **6**

Compound 6: To a solution of compound **5** (1.05 g, 1.93 mmol) in anhydrous DMF (10 mL) was added CH_3I (1.92 mL, 30.88 mmol) followed by Ag_2O (1.79 g, 7.72 mmol), and the mixture was stirred at 60 ^oC for 10 h wrapped in aluminum foil. The saturated Na_2SO_3 was added and the aqueous was extracted with EtOAc (50 mL × 3), The combined organic layer was washed with brine and dried over Na_2SO_4. Purification by FCC (PE-EtOAc, 6 : 1) afforded the product **6** (894 mg, 83% yield) as yellow foam: $[\alpha]^{20}_D$ +48.6 (*c* 1.30, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) Mixture of rotamers δ 8.22 (d, *J* = 8.0 Hz, 1 H), 7.66 (d, *J* = 8.0 Hz, 1 H), 7.46 (s, 0.4 H), 7.36 (s, 0.6 H), 6.95 (t, *J* = 8.0 Hz, 1 H), 5.02 (dd, *J* = 10.8, 3.6 Hz, 1 H), 3.87 (dd, *J* = 15.2, 3.6 Hz, 0.6 H), 3.79 (dd, *J* = 15.2, 3.6 Hz, 0.4 H), 3.76 (s, 3 H), 3.37 (dd, *J* = 15.2, 10.8 Hz, 0.4 H), 2.97 (dd, *J* = 15.2, 10.8 Hz, 0.6 H), 2.74 (s, 1.8 H), 2.69 (s, 1.2 H), 1.62 (s, 9 H), 1.40 (s, 3.6 H), 1.13 (s, 5.4 H); ^{13}C NMR (100 MHz, $CDCl_3$) Mixture of rotamers δ 171.6, 171.3, 155.6, 155.0, 148.6, 136.4, 134.3, 130.7, 126.6, 126.1, 125.4, 125.3, 116.7, 116.4, 115.3, 115.2, 84.3, 84.1, 83.8, 79.9, 79.8, 60.4, 59.2, 52.1, 33.0, 32.1, 28.2, 28.0, 27.8, 24.9; IR (KBr) 2978, 1741, 1697, 1157 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{23}H_{32}N_2O_6I$ $(M + H)^+$ 559.1300; found 559.1305.



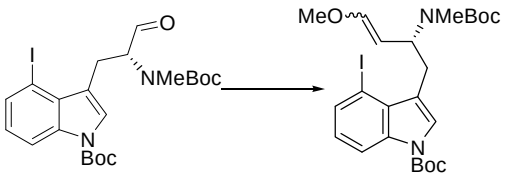
6 **13** **7**

Compound 7: To a solution of compound **6** (760 mg, 1.36 mmol) in THF (7 mL) at 0 ℃ was added $LiBH_4$[1] (74.1 mg, 3.41 mmol) portionwise and the mixture was stirred 5 h at room temperature. The reaction was quenched by the addition of saturated aqueous $NaHCO_3$ and the resulting solution was extracted with EtOAc (2 × 40 mL). The combined organic phase was

[1] Diaba, F.; Ricou, E.; Bonjoch, J. *Tetrahedron: Asymmetry* **2006,** *17,* 1437–1443.

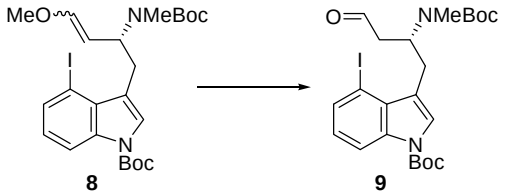
washed with brine and dried over Na_2SO_4. Purification by FCC (PE-EtOAc, 3 : 1) afforded the alcohol **13** (679 mg, 94% yield) as colorless foam: $[\alpha]^{20}_D$ +37.2 (*c* 1.60, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) Mixture of rotamers δ 8.24 (d, *J* = 8.0 Hz, 1 H), 7.70 (d, *J* = 8.0 Hz, 1 H), 7.48 (s, 0.5 H), 7.36 (s, 0.5 H), 6.96 (t, *J* = 8.0 Hz, 1 H), 4.66 (m, 0.5 H), 4.28 (m, 0.5 H), 3.81 (m, 2 H), 3.16-3.33 (m, 2 H), 2.84 (s, 1.5 H), 2.66 (s, 1.5 H), 1.64 (s, 9 H), 1.45 (s, 4.5 H), 1.03 (s, 4.5 H); ^{13}C NMR (100 MHz, $CDCl_3$) Mixture of rotamers δ 157.0, 156.3, 148.8, 136.5, 134.4, 130.8, 126.0, 125.4, 117.5, 117.3, 115.3, 84.5, 84.3, 84.1, 83.9, 79.7, 79.4, 63.7, 62.7, 60.0, 58.4, 33.0, 28.4, 28.1, 28.0, 27.7, 23.9; IR (KBr) 3435, 2977, 1738, 1688, 1157 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{22}H_{32}N_2O_5I$ $(M + H)^+$ 531.1350; found 531.1356.

Oxalyl chloride (179 μL, 2.12 mmol) was added dropwise to a solution of DMSO (250 μL, 3.53 mmol) in dry DCM (5 mL) at -78 °C. The reaction mixture was stirred at -78 °C for 20 min, and a solution of the above alcohol **13** (748 mg, 1.41 mmol) in dry DCM (10 mL) was added dropwise. The reaction mixture was stirred at -78 °C for another 45 min, followed by addition of Et_3N (978 μL, 7.05 mmol) at the same temperature. The cooling bath was then removed, and the reaction was stirred at room temperature for 1 h. Then saturated aqueous NH_4Cl was added, and the aqueous phase was extracted with DCM (50 mL × 3). The combined organic phases were washed with brine and dried over Na_2SO_4. Purification with FCC (PE-EtOAc, 6 : 1) afforded the desired aldehyde **7** (656 mg, 88%) as colorless oil: $[\alpha]^{20}_D$ +71.5 (*c* 1.23, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) show the presence of two rotamers δ 9.72 (d, *J* = 9.6 Hz, 1 H), 8.22 (d, *J* = 8.0 Hz, 1 H), 7.66 (d, *J* = 8.0 Hz, 1 H), 7.41 (s, 0.4 H), 7.35 (s, 0.6 H), 6.96 (t, *J* = 8.0 Hz, 1 H), 4.68 (dd, *J* = 11.0 Hz, 4.0 Hz, 0.6 H), 4.46 (dd, *J* = 11.0 Hz, 4.0 Hz, 0.4 H), 3.95 (dd, *J* = 15.0 Hz, 4.0 Hz, 0.6 H), 3.86 (dd, *J* = 15.0 Hz, 4.0 Hz, 0.4 H), 3.14 (dd, *J* = 15.0 Hz, 11.0 Hz, 0.4 H), 2.79 (dd, *J* = 15.0 Hz, 11.0 Hz, 0.6 H), 2.71 (s, 1.8 H), 2.61 (s, 1.2 H), 1.62 (s, 9 H), 1.44 (s, 3.6 H), 1.19 (s, 5.4 H); ^{13}C NMR (100 MHz, $CDCl_3$) all rotamers shown δ 199.1, 199.0, 155.8, 155.0, 148.7, 148.6, 136.5, 134.4, 134.3, 130.7, 130.6, 126.8, 126.7, 125.6, 125.5, 116.7, 116.2, 115.4, 115.3, 84.3, 84.2, 84.0, 80.7, 80.3, 67.8, 67.6, 35.4, 34.1, 28.2, 28.0, 27.8, 22.8, 22.6; IR (KBr) 2978, 2723, 1738, 1370 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{22}H_{29}N_2O_5INa$ $(M + Na)^+$ 551.1013; found 551.1019.



7 **8**

Compound 8: Methoxymethyltriphenyl phosphonium chloride (889 mg, 2.59 mmol) was suspended in dried THF (2 mL), and cooled to -78 °C under an argon atmosphere. KHMDS (3.4 mL, 2.38 mmol, 0.7 M in toluene) was added slowly, then the resulting mixture was stirred at 0 °C for 0.5 h. Aldehyde **7** (380 mg, 0.72 mmol) was dissolved in dried THF (4 mL), and added dropwise to the former mixture solution via syringe at -78 °C. After stirring at room temperature for 4 h, the reaction mixture was quenched with saturated aqueous NH_4Cl followed by addition of EtOAc (10 mL). The organic layer was separated, and the aqueous phase was further extracted with EtOAc (2 × 50 mL). The combined organic phases were dried over Na_2SO_4. After removal of the solvent in vacuo, the residue was purified by column chromatography on silica gel (PE-EtOAc, 5 : 1) to give the vinyl ether **8** (*Z*/*E* = 5 : 4, 344 mg, 86%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21 (d, *J* = 8.0 Hz, 1 H × 2), 7.67-7.70 (m, 1 H × 2), 7.35-7.48 (m, 1 H × 2), 6.91-6.97 (m, 1 H × 2), 6.56 (d, *J* = 12.0 Hz (*E*), 1 H), 5.97 (d, *J* = 6.1 Hz (*Z*), 1 H), 5.02-5.31 (m, 1 H × 2), 4.49-4.88 (m, 1 H × 2), 3.57 (s, 3 H × 2), 3.37-3.42 (m, 1 H × 2), 2.87-3.23 (m, 1 H × 2), 2.75 (s, 3 H × 2), 1.63 (s, 9 H × 2), 1.03-1.39 (m, 9 H × 2); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.5, 149.8, 149.0, 148.9, 148.1, 136.4, 134.4, 131.3, 131.0, 125.9, 125.3, 125.1, 118.1, 117.7, 115.3, 115.2, 104.9, 101.8, 84.6, 83.8, 79.0, 78.7, 59.8, 56.0, 51.7, 29.0, 28.1; IR (KBr) 3450, 2976, 1736, 1650, 1053 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{24}H_{33}N_2O_5INa$ $(M + Na)^+$ 579.1326; found 579.1328.

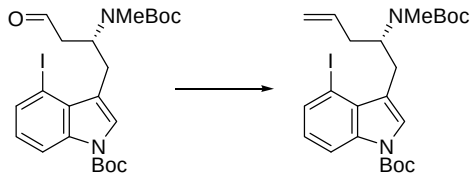


8 **9**

Compound 9[2]: To a solution of **8** (390 mg, 0.70 mmol) in THF/H_2O (10 : 1, 14 mL) was slowly added $Hg(OAc)_2$ (671 mg, 2.10 mmol) at 0 °C. After stirring for 4.5 h at ambient temperature, excess saturated aqueous solution of KI (2 mL) was added at 0 °C. The resulting reaction mixture

[2] (a) Ansell, M. F.; Caton, M. P. L.; Stuttle, K. A. J. *J. Chem. Soc., Perkin Trans. 1* **1984**, 1069–1077. (b) Clive, D. J.; Li, Z.; Yu, M. *J. Org. Chem.* **2007**, *72*, 5608–5617.

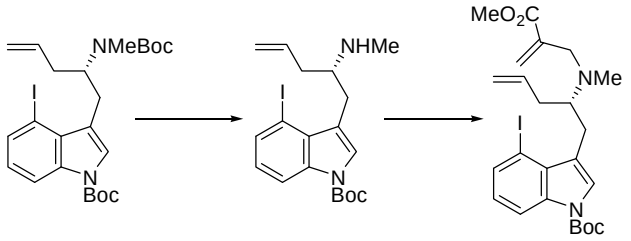
was stirred for additional 20 min at ambient temperature, and then extracted with EtOAc (2 × 30 mL). The combined extracts were dried over Na_2SO_4, and concentrated under reduced pressure. Purification of the residue through column chromatography on silica gel (PE-EtOAc, 4 : 1) afforded the aldehyde **9** as yellow foam (361 mg, 95%): $[\alpha]^{20}_D$ +48.7 (*c* 1.20, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) Mixture of rotamers δ 9.72 (s, 1 H), 8.23 (d, *J* = 8.0 Hz, 1 H), 7.70 (d, *J* = 8.0 Hz, 1 H), 7.49 (s, 0.4 H), 7.36 (s, 0.6 H), 6.97 (t, *J* = 8.0 Hz, 1 H), 5.10 (m, 0.6 H), 4.90 (m, 0.4 H), 2.94-3.36 (m, 2 H), 2.67-2.83 (m, 2 H), 2.67-2.77 (m, 3 H), 1.63 (s, 9 H), 1.39 (s, 4 H), 1.06 (s, 5 H); ^{13}C NMR (100 MHz, $CDCl_3$) Mixture of rotamers δ 200.6, 200.0, 155.5, 155.3, 148.7, 136.5, 134.6, 134.4, 130.6, 126.4, 126.3, 125.5, 117.2, 116.9, 115.5, 115.3, 84.5, 84.3, 84.0, 79.7, 79.5, 52.6, 52.3, 46.4, 46.3, 31.6, 28.3, 28.1, 27.8; IR (KBr) 2977, 2726, 1733, 1393 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{23}H_{32}N_2O_5I$ $(M+H)^+$ 543.1350; found 543.1358.



9 **10**

Compound 10: Methyltriphenyl phosphonium bromide (262 mg, 0.73 mmol) was suspended in dried THF (3 mL), and cooled to 0 ^oC under an argon atmosphere. *t*-BuOK (66.0 mg, 0.59 mmol) was added, then the resulting mixture was stirred at room temperature for 0.5 h. Aldehyde **9** (159 mg, 0.29 mmol) was dissolved in dried THF (6.6 mL), and added dropwise to the former mixture solution via syringe at 0 ^oC. After stirring at room temperature for additional 20 min, the reaction mixture was quenched with saturated aqueous NH_4Cl followed by addition of EtOAc (5 mL). The organic layer was separated, and the aqueous phase was further extracted with EtOAc (2 × 30 mL). The combined organic phases were dried over Na_2SO_4. After removal of the solvent in vacuo, the residue was purified by column chromatography on silica gel (PE-EtOAc, 6 : 1) to give the product **10** as colorless oil (146 mg, 92%): $[\alpha]^{20}_D$ +29.1 (*c* 2.50, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) Mixture of rotamers δ 8.22 (m, 1 H), 7.68 (m, 1 H), 7.52 (s, 0.3 H), 7.32 (s, 0.7 H), 6.91-6.97 (m, 1 H), 5.72-5.88 (m, 1 H), 5.10 (d, *J* = 17.1 Hz, 1 H), 5.03 (d, *J* = 10.0 Hz, 1 H), 4.63 (m, 1 H), 3.11-3.34 (m, 1.4 H), 2.74 (s, 2 H), 2.61-2.69 (m, 0.6 H), 2.67 (s, 1 H), 2.35-2.44 (m, 2 H), 1.63 (s, 9 H), 1.39 (s, 3 H), 1.01 (s, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) Mixture of rotamers δ

156.0, 155.8, 148.9, 148.8, 136.4, 135.4, 135.0, 134.4, 134.3, 130.9, 126.0, 125.6, 125.3, 125.2, 118.0, 117.9, 116.8, 115.3, 115.2, 84.7, 84.4, 84.1, 83.7, 78.9, 37.1, 36.9, 28.4, 28.1, 27.8; IR (KBr) 3076, 2976, 1643, 748 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{24}H_{34}N_2O_4I$ $(M+H)^+$ 541.1558; found 541.1548.



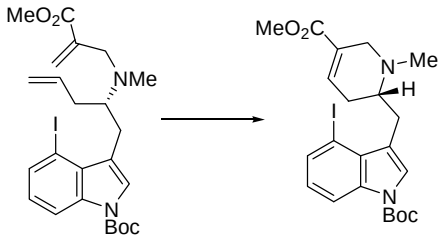
10 **14** **4**

Compound 4: To a stirred solution of **10** (281 mg, 0.52 mmol) and 2, 6-lutidine (302 μL, 2.60 mmol) in DCM (10.5 mL) at 0 ^oC was added TMSOTf[3] (377 μL, 2.08 mmol) dropwise. The reaction mixture was stirred at 0 ^oC for 20 min, and sat. aq. $NaHCO_3$ was added followed by extraction with CH_2Cl_2 (2 × 30 mL). The combined organic phases were washed with brine and dried over Na_2SO_4. Purification by FCC (DCM-MeOH, 20 : 1) afforded the amine **14** (217 mg, 95%) as colorless oil: $[\alpha]^{20}_D$ +8.5 (*c* 1.41, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 8.24 (d, J = 8.0 Hz, 1 H), 7.69 (d, J = 8.0 Hz, 1 H), 7.57 (s, 1 H), 6.97 (t, J = 8.0 Hz, 1 H), 5.92 (dt, J = 7.2 Hz, 16.8 Hz, 1 H), 5.17 -5.22 (m, 2 H), 3.35-3.37 (m, 1 H), 3.15-3.27 (m, 2 H), 2.59 (s, 3 H), 2.46 (m, 2 H), 1.65 (s, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.8, 136.5, 134.5, 134.1, 130.7, 126.8, 125.5, 118.3, 117.3, 115.3, 84.6, 84.2, 58.6, 36.4, 33.1, 29.1, 28.1; IR (KBr) 3337, 2921, 1737, 1158 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{19}H_{26}N_2O_2I$ $(M+H)^+$ 441.1034; found 441.1042.

To a mixture of the above amine[4] **14** (128 mg, 0.29 mmol) and potassium carbonate (200.7 mg, 1.45 mmol) in acetonitrile (3 mL) was added 2-(bromomethyl)acrylic acid methyl ester[5] (260 mg, 1.45 mmol), and the mixture was heated at 60 ^oC for 12 h. Quenched with saturated aqueous NH_4Cl followed by addition of EtOAc (5 mL). The organic layer was separated, and the aqueous phase was further extracted with EtOAc (2 × 30 mL). The combined organic phases were dried

[3] Xu, Z.; Li, Q.; Zhang, L.; Jia, Y. *J. Org. Chem.* **2009**, *74*, 6859–6862.
[4] Matsumura, Y.; Aoyagi, S.; Kibayashi, C. *Org. Lett.* **2004**, *6*, 965–968.
[5] Borrell, J.; Teixidó, J.; Martínez-Teipel, B. Matallana, J. L.; Copete, M. T.; Llimargas, A.; García, E. *J. Med. Chem.* **1998,** *41,* 3539-3545.

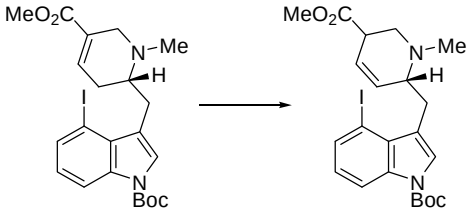
over Na_2SO_4. Purification by FCC (DCM-MeOH, 40 : 1) afforded the product **4** (125 mg, 80%) as colorless oil: $[\alpha]^{20}_D$ +6.4 (*c* 1.86, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22 (d, *J* = 8.0 Hz, 1 H), 7.68 (d, *J* = 8.0 Hz, 1 H), 7.47 (s, 1 H), 6.94 (t, *J* = 8.0 Hz, 1 H), 6.16 (s, 1 H), 5.88 (dt, *J* = 7.2 Hz, 16.8 Hz, 1 H), 5,69 (s, 1 H), 5.05 (d, *J* = 17.2 Hz, 1 H), 4.99 (d, *J* = 10.4 Hz, 1 H), 3.67 (s, 3 H), 3.45 (d, *J* = 15.6 Hz, 1 H), 3.34 (d, *J* = 15.6 Hz, 1 H), 3.14-3.24 (m, 2 H), 3.01 (dd, *J* = 7.2 Hz, 15.2 Hz, 1 H), 2.41-2.48 (m, 1 H), 2.31 (s, 3 H), 2.14-2.21 (m, 1 H), 1.65 (s, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.6, 149.0, 138.1, 137.3, 136.2, 134.5, 131.3, 126.2, 125.5, 125.1, 119.3, 115.9, 115.2, 84.6, 83.8, 63.6, 54.2, 51.6, 36.5, 34.7, 28.1, 26.7; IR (KBr) 3437, 2977, 1731, 1158, 912 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{24}H_{32}N_2O_4I$ $(M+H)^+$ 539.1401; found 539.1405.



4 **3**

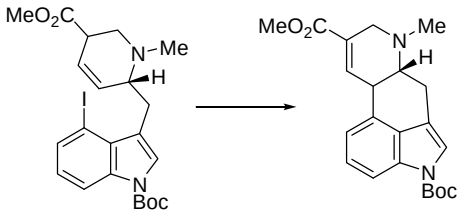
Compound 3[6]: To a degassed solution of the diene **4** (111 mg, 0.21 mmol) in toluene (20.5 mL) was added TsOH (39.0 mg, 0.23 mmol) followed by heating of the mixture to 50 °C for 30 min. Then, the Grubbs II catalyst (5 mol%) was added and the mixture was stirred for 10 h at 55 °C. Then, saturated Na_2CO_3 solution was added and the resulting mixture was extracted with EtOAc (2 × 30 mL). The combined organic phases were washed with brine and dried over Na_2SO_4. Purification by FCC (PE-Actone, 3 : 1) afforded the product **3** (92 mg, 88%) as brown oil: $[\alpha]^{20}_D$ -12.8 (*c* 1.88, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20 (d, *J* = 8.0 Hz, 1 H), 7.68 (d, *J* = 8.0 Hz, 1 H), 7.45 (s, 1 H), 6.92-6.97 (m, 2 H), 3.74 (s, 3 H), 3.35-3.54 (m, 3 H), 3.23 (m, 1 H), 2.74 (dd, *J* = 10.0 Hz, 14.4 Hz, 1 H), 2.56 (s, 3 H), 2.21 (m, 2 H), 1.66 (s, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.4, 148.9, 137.2, 136.3, 134.6, 130.9, 128.0, 126.0, 125.3, 118.2, 115.3, 84.7, 84.2, 56.6, 51.5, 51.2, 40.6, 28.1, 25.7; IR (KBr) 3437, 2977, 1731, 1158, 912 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{22}H_{28}N_2O_4I$ $(M+H)^+$ 511.1088; found 511.1077.

[6] Prusov, E.; Maier, M. E. *Tetrahedron* **2007**, *63*, 10486–10496.



3 **2**

Compound 2[7]**:** To a stirred solution of 2, 2, 6, 6-tetramethylpiperidine (106 μL, 0.62 mmol) in THF (1 mL) was added *n*-BuLi (370 μL, 0.60 mmol, 1.6 M in hexanes) at 0 ºC. After stirring for 30 min at room temperature, the mixture was cooled to -78 °C. Compound **3** (60 mg, 0.12 mmol) was dissolved in dried THF (1.5 mL), and added dropwise to the former mixture solution via syringe. After stirring for 40 min, 2, 6-di(*t*-Bu)phenol (145.6 mg, 0.7 mmol) in THF was added. The reaction mixture was then allowed to warm to 0 ºC and stirred for 20 min. Quenched with saturated aqueous NH_4Cl followed by addition of EtOAc (5 mL). The organic layer was separated, and the aqueous phase was further extracted with EtOAc (2 × 30 mL). The combined organic phases were dried over Na_2SO_4. Purification by FCC (PE-Actone, 6 : 1) afforded the mixed epimers **2** (50 mg, 84%) as yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21 (d, J = 8.0 Hz, 1 H × 2), 7.68-7.70 (m, 1 H × 2), 7.59 (s, 1 H), 7.51 (s, 1 H), 6.92-6.97 (m, 1 H × 2), 5.88-5.93 (m, 1 H × 2), 5.68-5.77 (m, 1 H × 2), 3.74 (s, 3 H), 3.71 (s, 3 H), 3.19-3.58 (m, 4 H × 2), 2.68-3.00 (m, 2 H × 2), 2.55 (s, 3 H), 2.54 (s, 3 H), 1.66 (s, 9 H × 2); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.6, 173.0, 149.0, 148.9, 136.3, 136.2, 134.6, 134.5, 131.2, 131.1, 130.6, 130.4, 126.6, 126.5, 125.3, 125.2, 123.2, 122.7, 117.9, 117.4, 115.3, 84.7, 84.6, 84.1, 84.0, 60.9, 60.1, 53.9, 52.0, 51.9, 50.0, 43.0, 42.7, 41.5, 38.0, 29.0, 28.7, 28.2; HRMS (ESI) *m/z* calcd for $C_{22}H_{28}N_2O_4I$ $(M+H)^+$ 511.1088; found 511.1097.

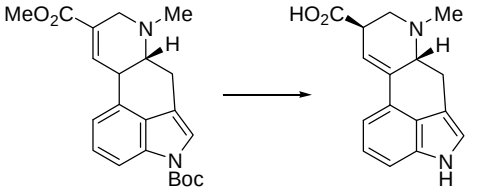


2 **11**

Compound 11[8]**:** Compound **2** (79 mg, 0.16 mmol) dissolved in dry CH_3CN (15 mL) was degassed for 30 min. PPh_3 (12.2 mg, 0.046 mmol), Ag_2CO_3 (85.5 mg, 0.31 mmol) and $Pd(OAc)_2$

[7] Inoue, T.; Yokoshima, S.; Fukuyama, T. *Heterocycles* **2009**, *79*, 373–378.
[8] Abelman, M. M.; Oh, T.; Overman, L. E. *J. Org. Chem.* **1987,** *52*, 4130–4133.

(3.5 mg, 0.015 mmol) were added to the reaction, and the resulting reaction mixture was heated at 82 ^{o}C under argon atmosphere for 2 h. After cooling, quenched with saturated aqueous NH_4Cl following by addition of EtOAc (5 mL). The organic layer was separated, and the aqueous phase was further extracted with EtOAc (2 × 30 mL). The combined organic phases were washed with brine and dried over Na_2SO_4. Purification by FCC (PE-Actone, 6 : 1) afforded the starting material **2** (27 mg, 34%) and the product **11** (33 mg, 84%, brsm) as yellow solid: $[\alpha]^{20}_{D}$ -165.9 (*c* 1.23, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (s, 1 H), 7.29-7.33 (m, 2 H), 7.13 (d, *J* = 7.28 Hz, 1 H), 7.05 (s, 1 H), 4.06 (s, 1 H), 3.71 (s, 3 H), 3.50 (d, *J* = 17.4 Hz, 1H), 3.35-3.39 (m, 2 H), 2.95 (m, 1 H), 2.70 (m, 1 H), 2.60 (s, 3 H), 1.66 (s, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.0, 150.1, 140.4, 133.5, 131.6, 129.0, 127.1, 125.6, 120.0, 119.8, 115.4, 113.5, 83.4, 57.3, 51.6, 48.8, 42.3, 39.3, 37.4, 28.2; IR (KBr) 3434, 2922, 1730, 1257, 1116, 802 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{44}H_{53}N_4O_8$ $(2M+H)^+$ 765.3858; found 765.3856.



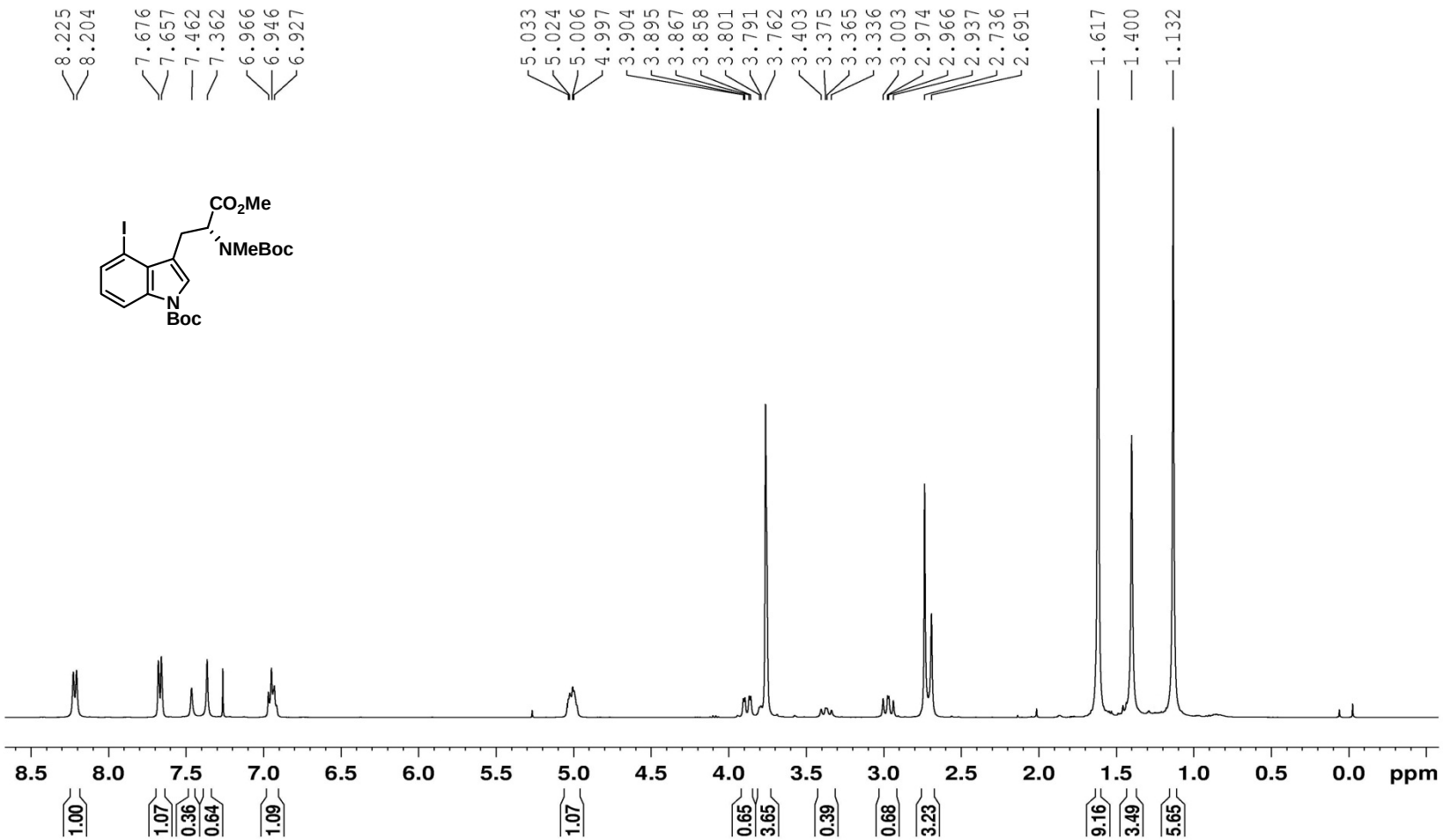
11 (+)-lysergic acid (**1**)

Compound 1[9]**:** To a solution of compound **11** (31 mg, 0.08 mmol) in ethanol (1 mL) was added 1 N KOH (1 mL). The reaction was heated at 70 ^{o}C for 3 h. The hot solution was treated with charcoal and filtered. The organic solvent was removed by evaporation. 1 N HCl solution was used to carefully adjust the pH to 5.8 at 0 °C until a solid was formed. The aqueous solution was removed and the precipitate was washed with cold water and acetone to give (+)-lysergic acid **1** as a pale brown amorphous solid (11.2 mg, 52% yield), in agreement with the reported data by Hendrickson and Ohno[10]: $[\alpha]^{20}_{D}$ +40 (*c* 0.50, pyridine); ^{1}H NMR (400 MHz, pyridine-d_5) of (+)-lysergic acid δ 11.66 (s, 1 H), 7.42 (d, *J* = 8.0 Hz, 1 H), 7.40 (d, *J* = 8.0 Hz, 1 H), 7.27 (t, *J* = 8.0 Hz, 1 H), 7.22 (s, 1 H), 7.15 (s, 1 H), 4.04 (m, 1 H), 3.61 (dd, *J* = 14.5, 5.5 Hz, 1 H), 3.52 (dd, *J* = 11.2, 5.0 Hz, 1 H), 3.29 (m, 1 H), 2.92 (m, 2 H), 2.51 (s, 3 H); ^{13}C NMR (100 MHz, pyridine-d_5) δ 175.1, 136.8, 136.1, 129.1, 127.4, 120.0, 119.8, 112.3, 110.6, 110.5, 63.8, 56.0, 43.9,

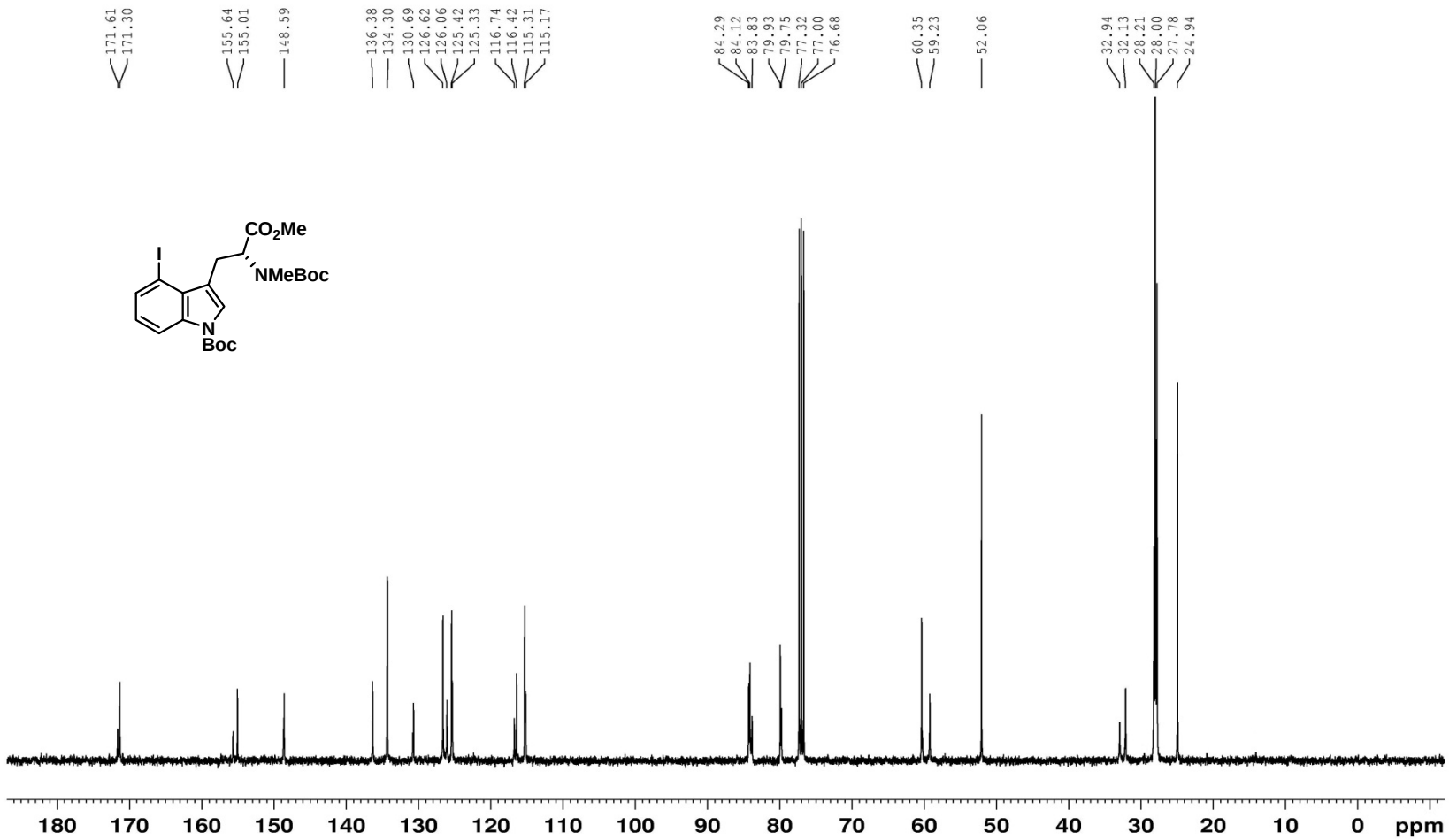
[9] Oppolzer, W.; Francotte, E.; Bättig, K. *Helv. Chim. Acta* **1981**, *64*, 478–481.
[10] (a) Hendrickson, J. B.; Wang, J. *Org. Lett.* **2004**, *6*, 3–5. (b) Inuki, S.; Iwata, A.; Oishi, S.; Fujii, N.; Ohno, H. *J. Org. Chem.* **2011**, *76*, 2072–2083.

43.5, 27.9 (one of the sp^2 carbons was overlapped with C_5D_5N solvent peaks); IR (KBr) 3400, 1595, 1453 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{16}H_{17}N_2O_2$ $(M+H)^+$ 269.1285; found 269.1285.

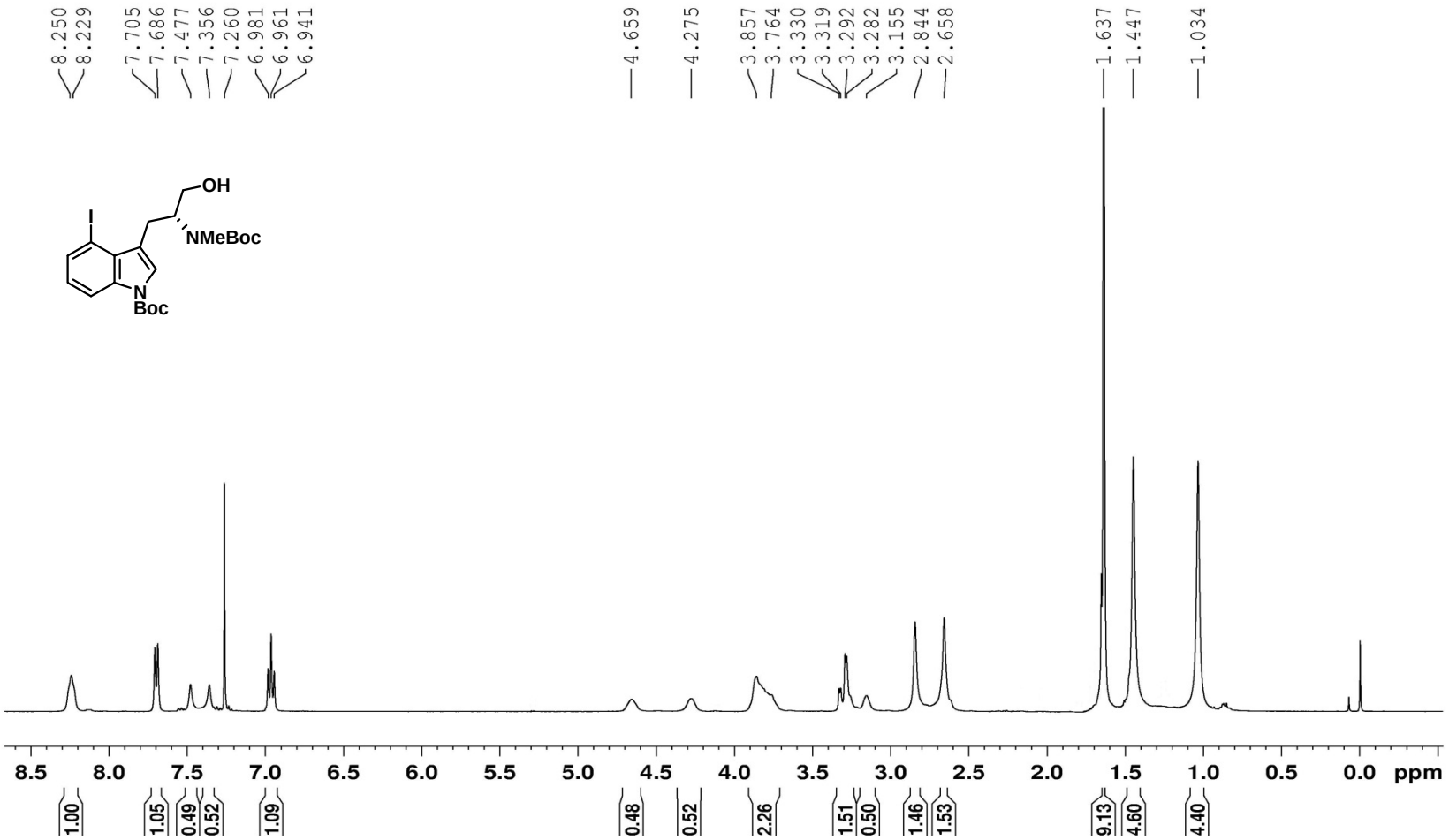
^{1}H-NMR of compound 6 (400 MHz, $CDCl_3$)



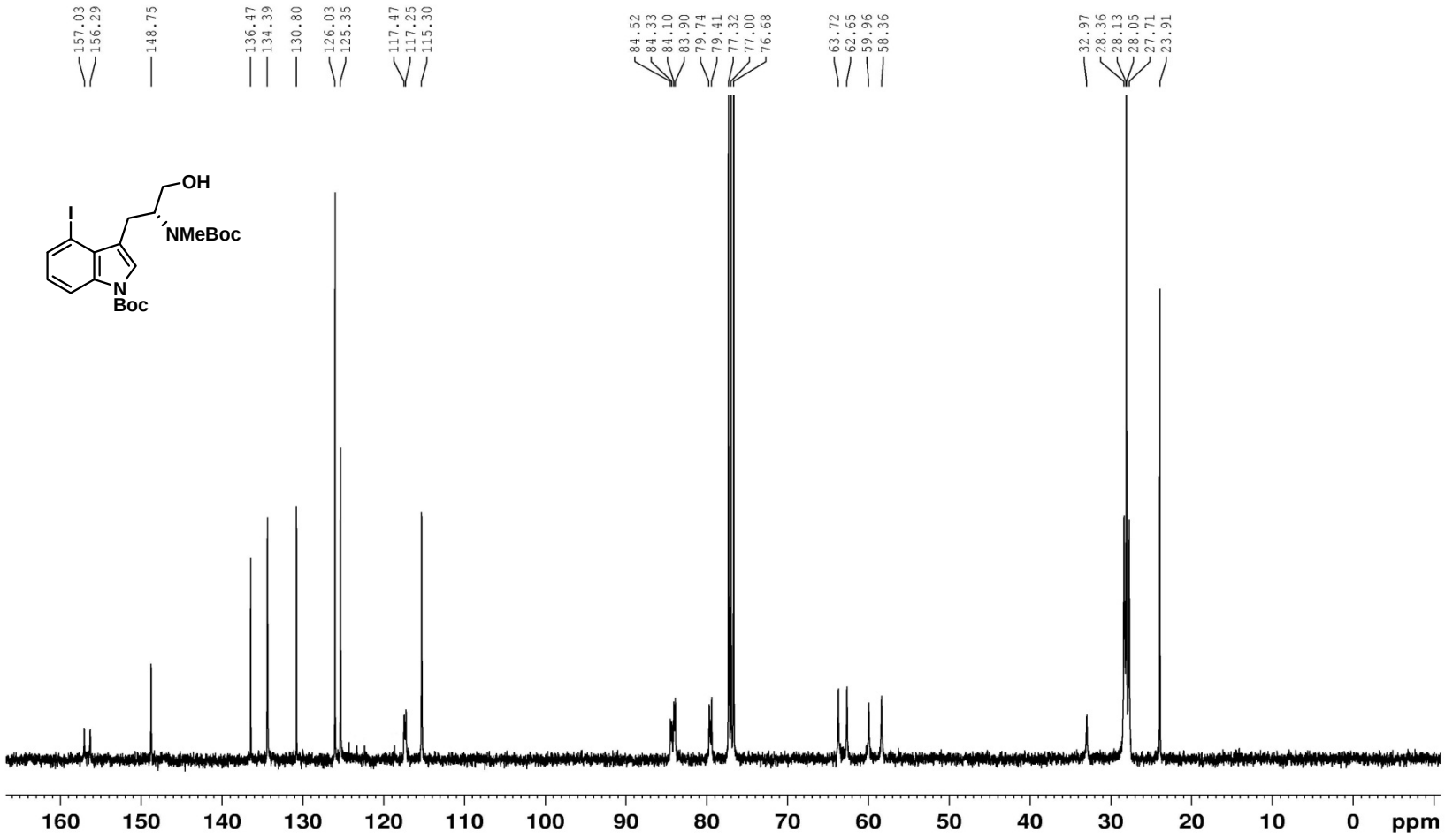
^{13}C-NMR of compound 6 (100 MHz, $CDCl_3$)



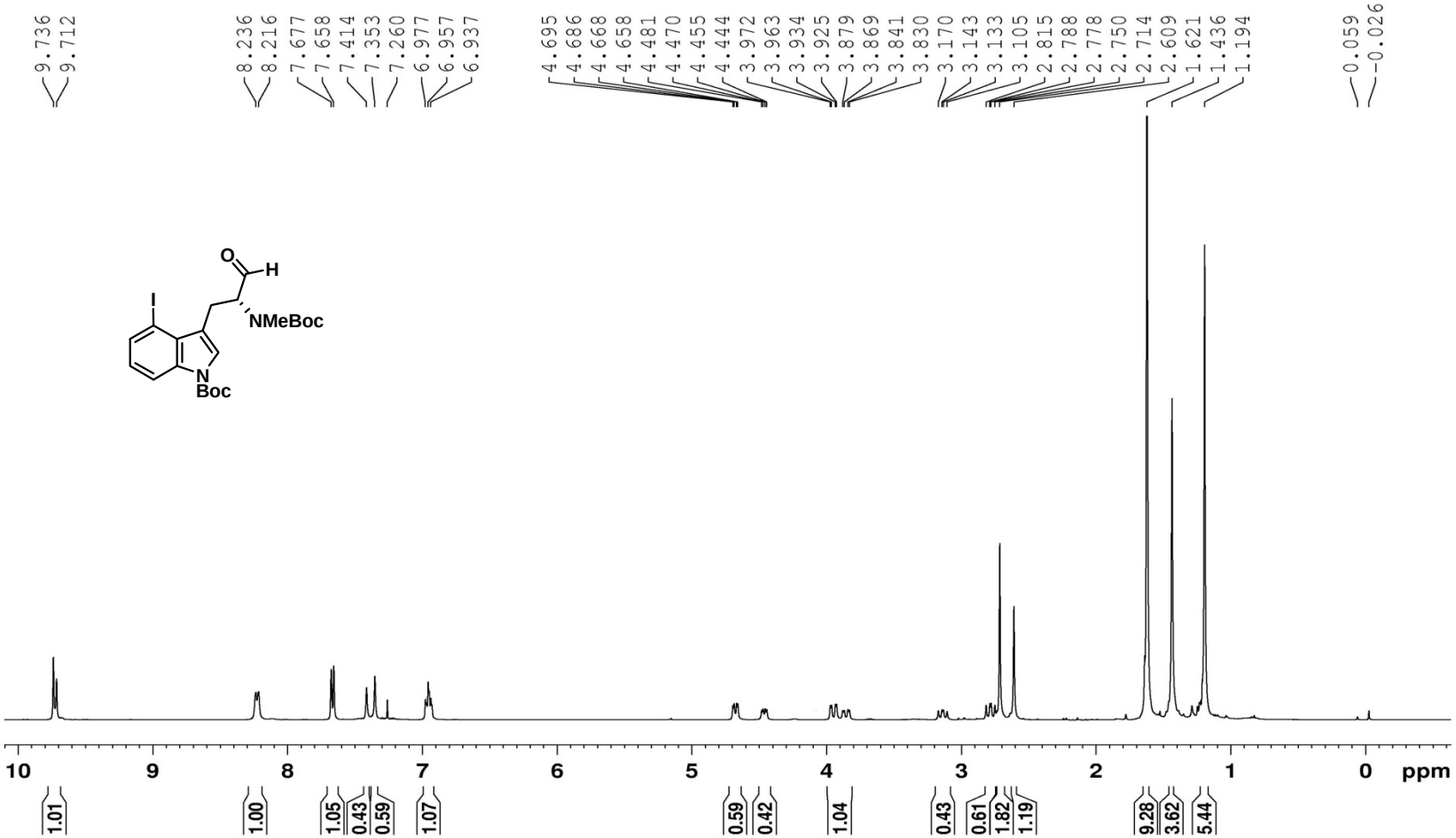
^{1}H-NMR of compound 13 (400 MHz, $CDCl_3$)



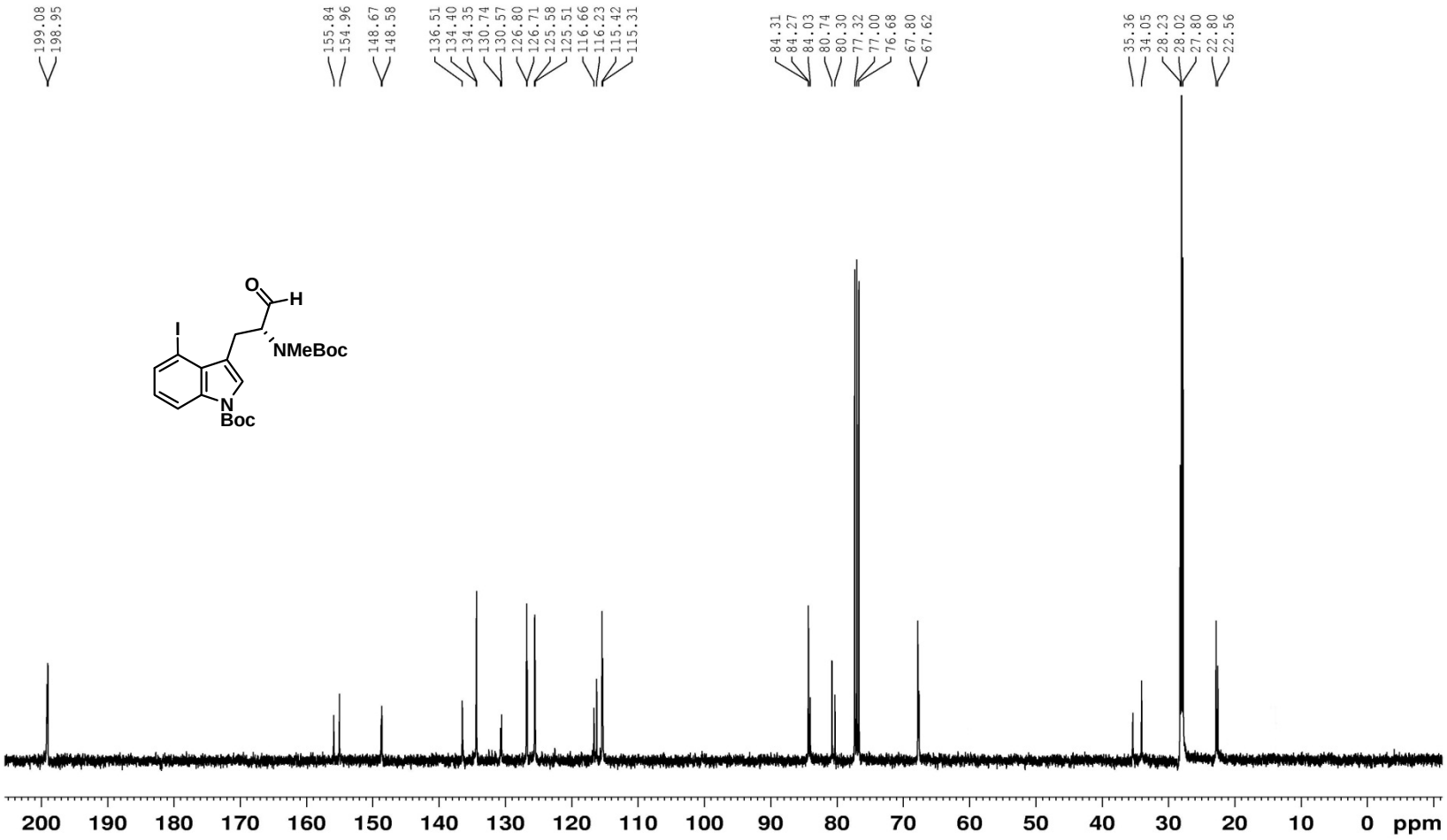
^{13}C-NMR of compound 13 (100 MHz, $CDCl_3$)



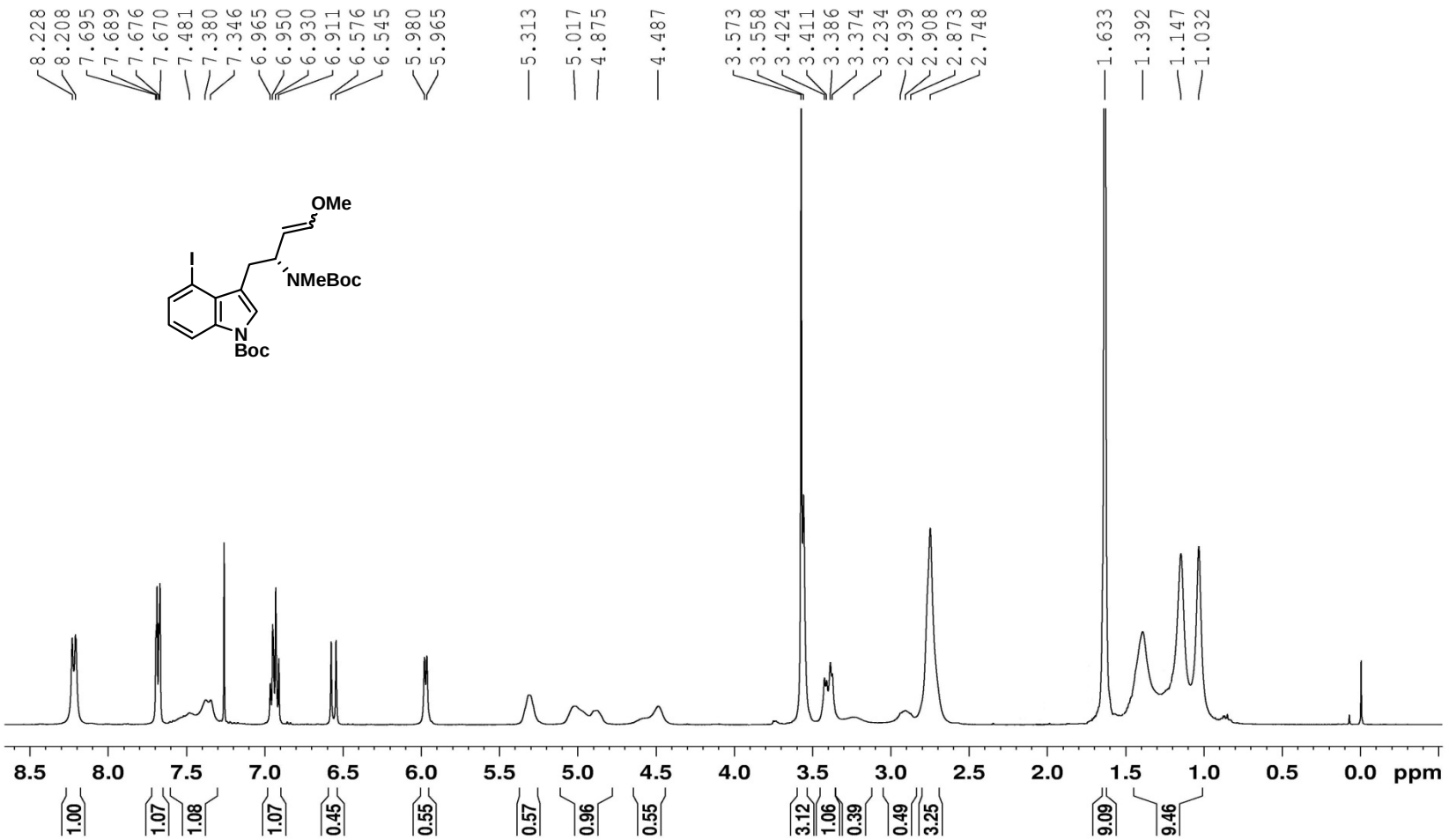
^{1}H-NMR of compound 7 (400 MHz, $CDCl_3$)



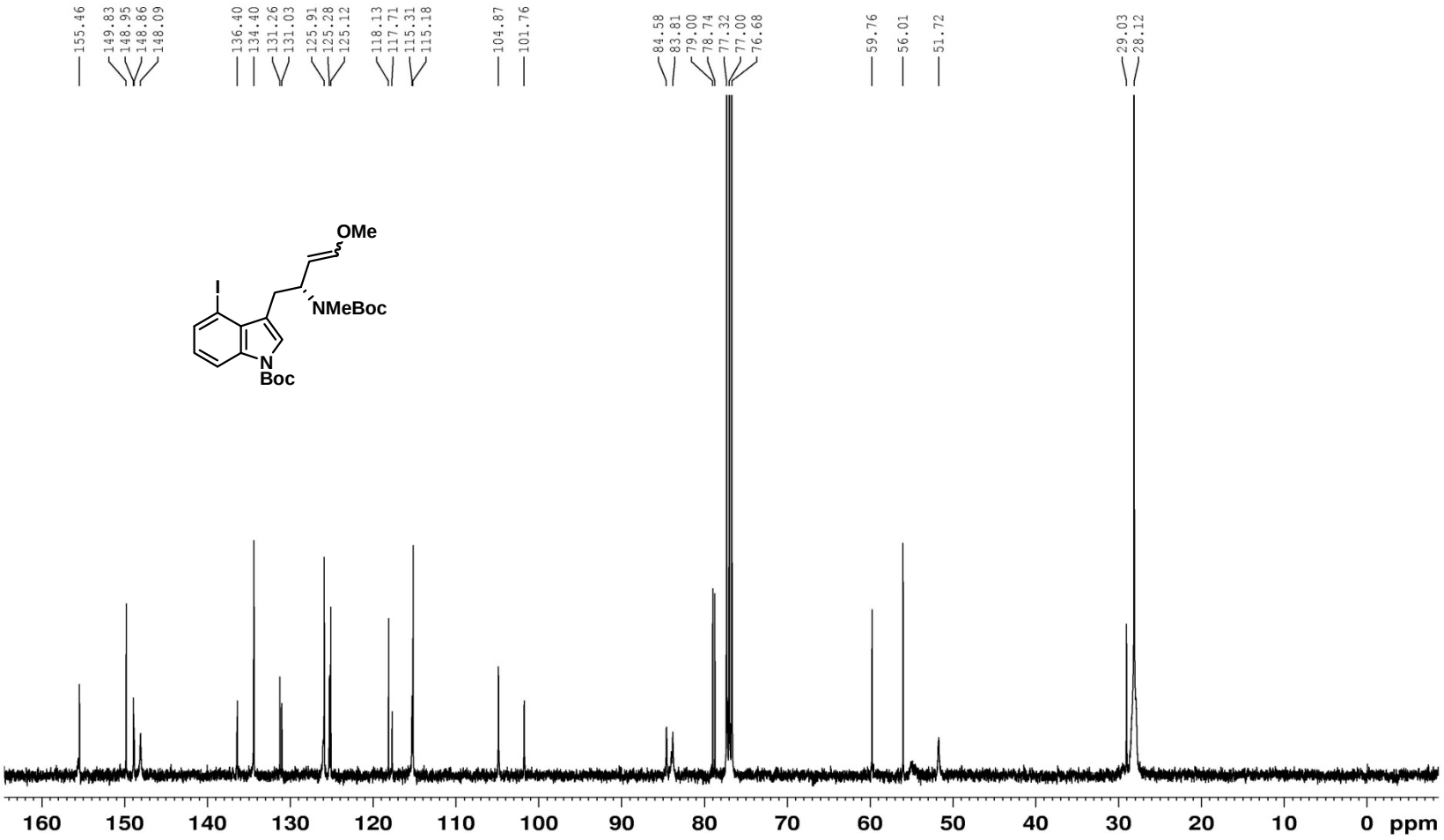
^{13}C-NMR of compound 7 (100 MHz, $CDCl_3$)



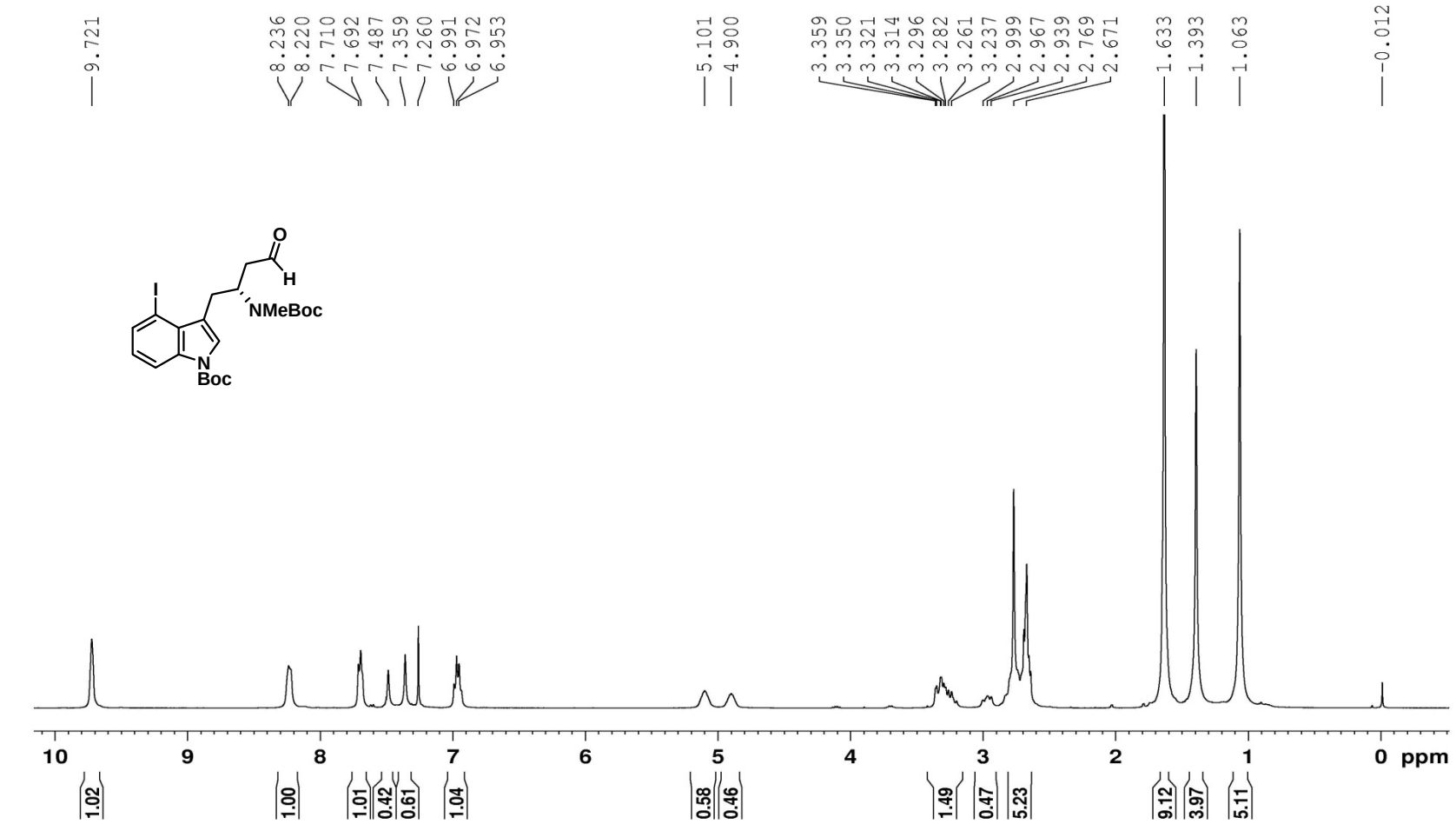
^{1}H-NMR of compound 8 (400 MHz, $CDCl_3$)



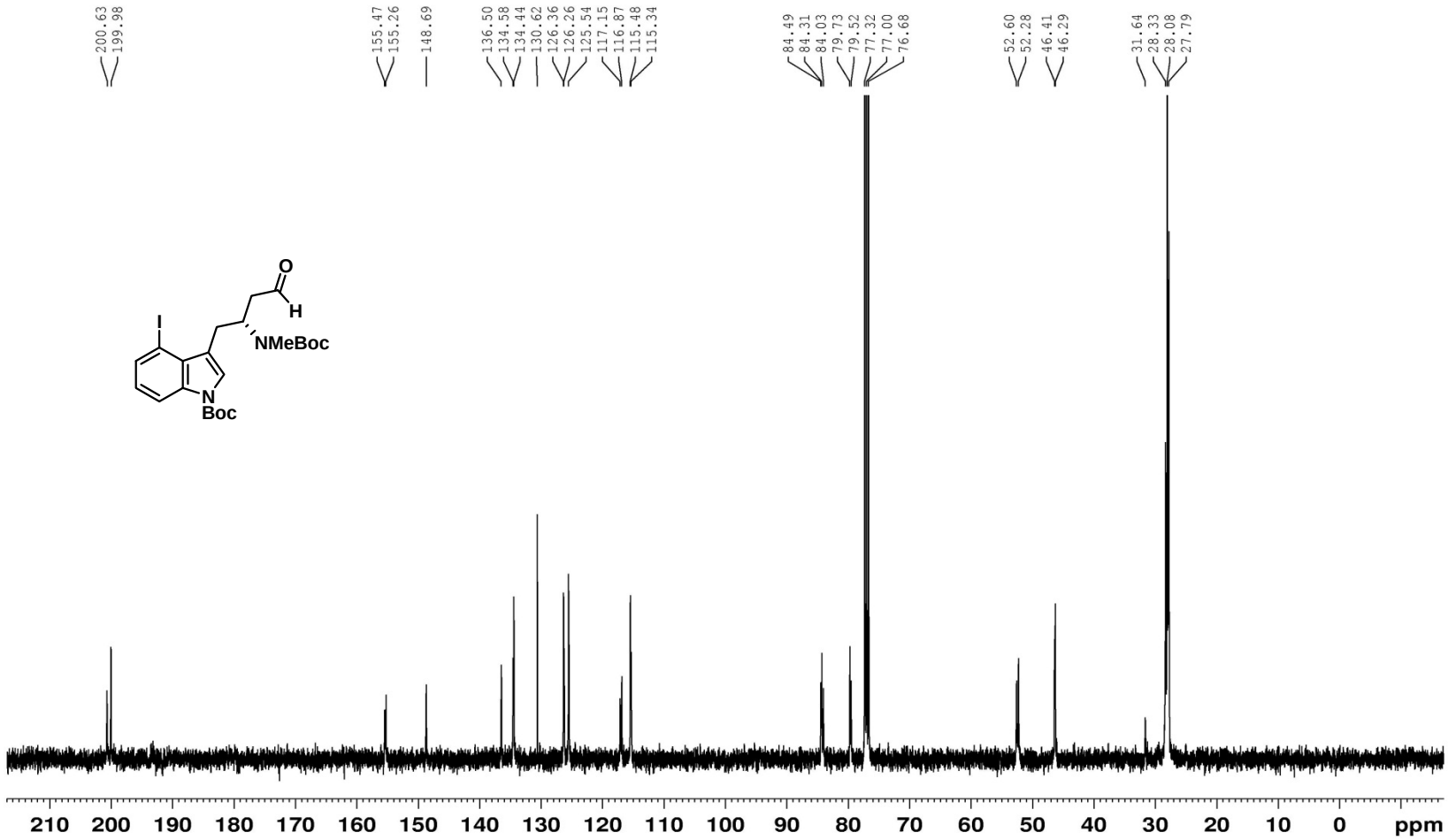
^{13}C-NMR of compound 8 (100 MHz, $CDCl_3$)



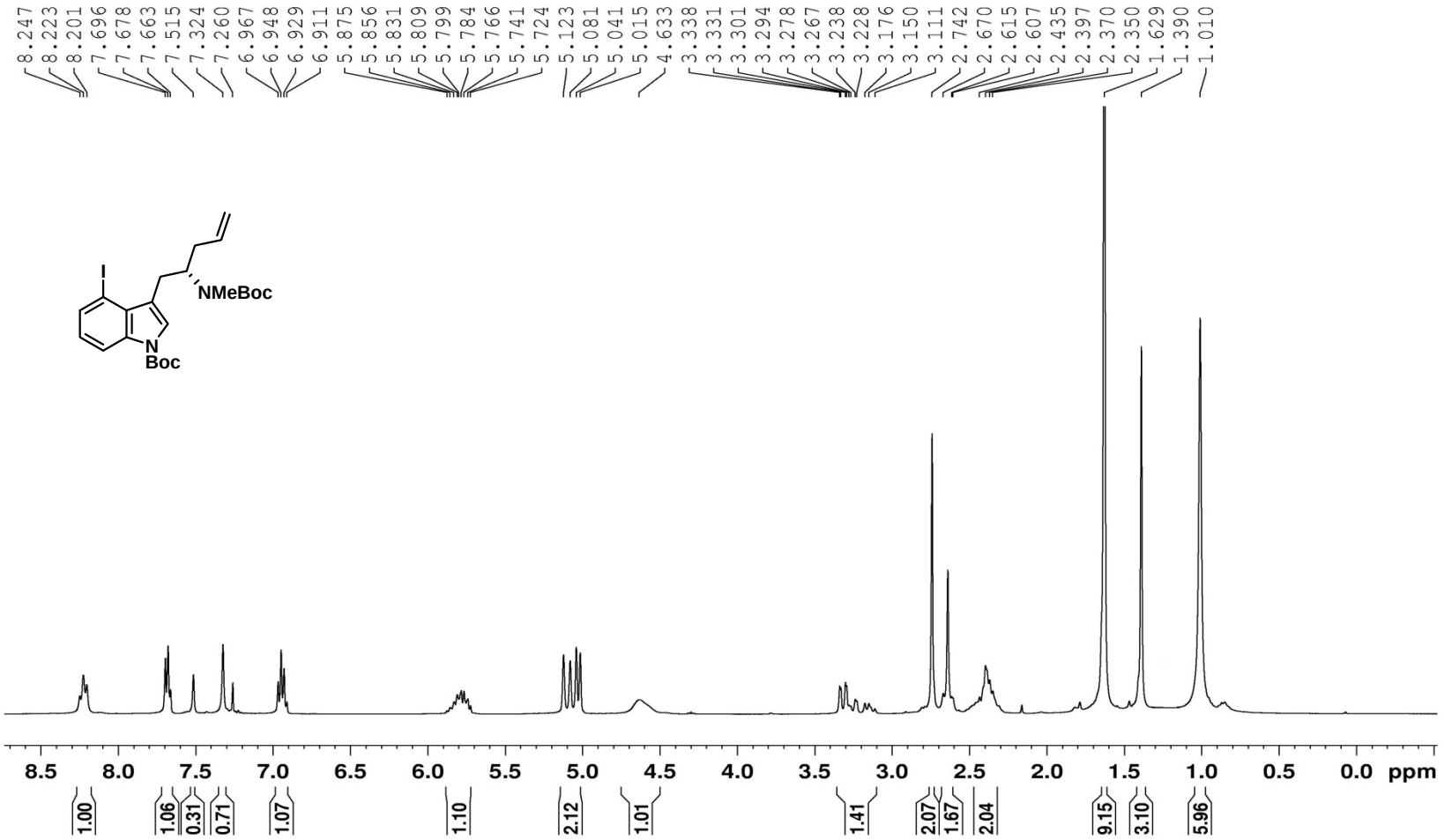
^{1}H-NMR of compound 9 (400 MHz, $CDCl_3$)



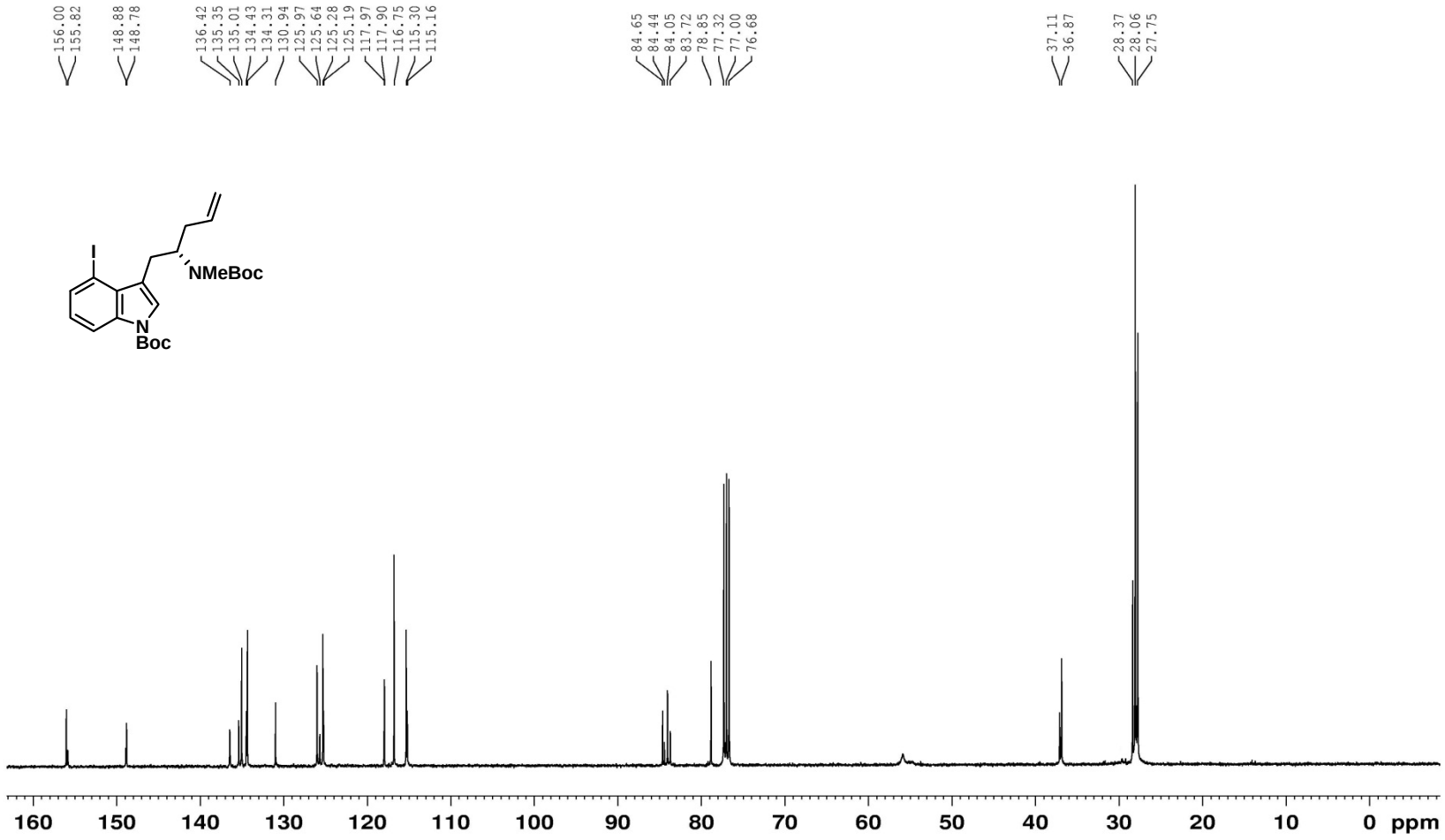
^{13}C-NMR of compound 9 (100 MHz, $CDCl_3$)



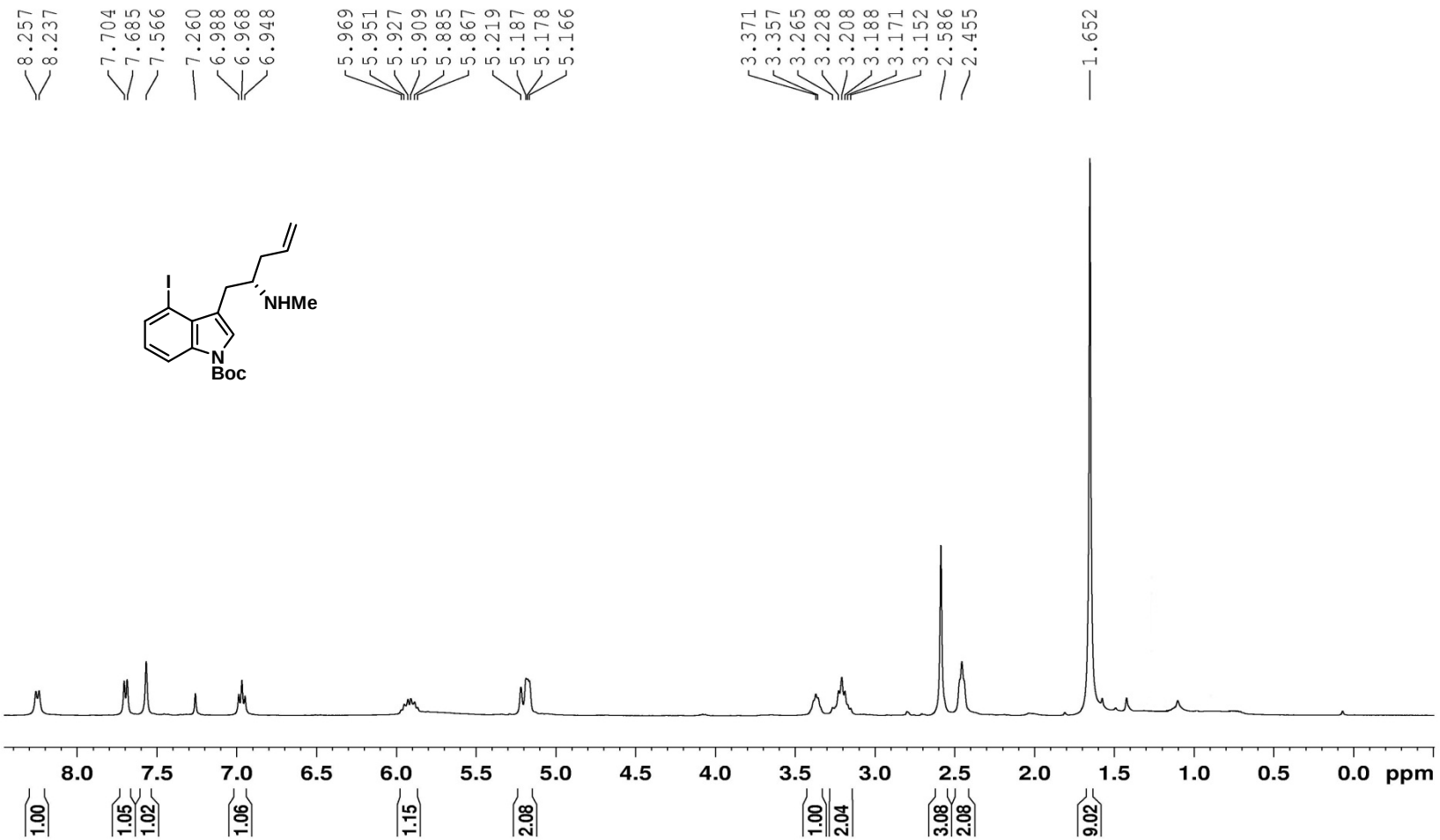
^{1}H-NMR of compound 10 (400 MHz, $CDCl_3$)



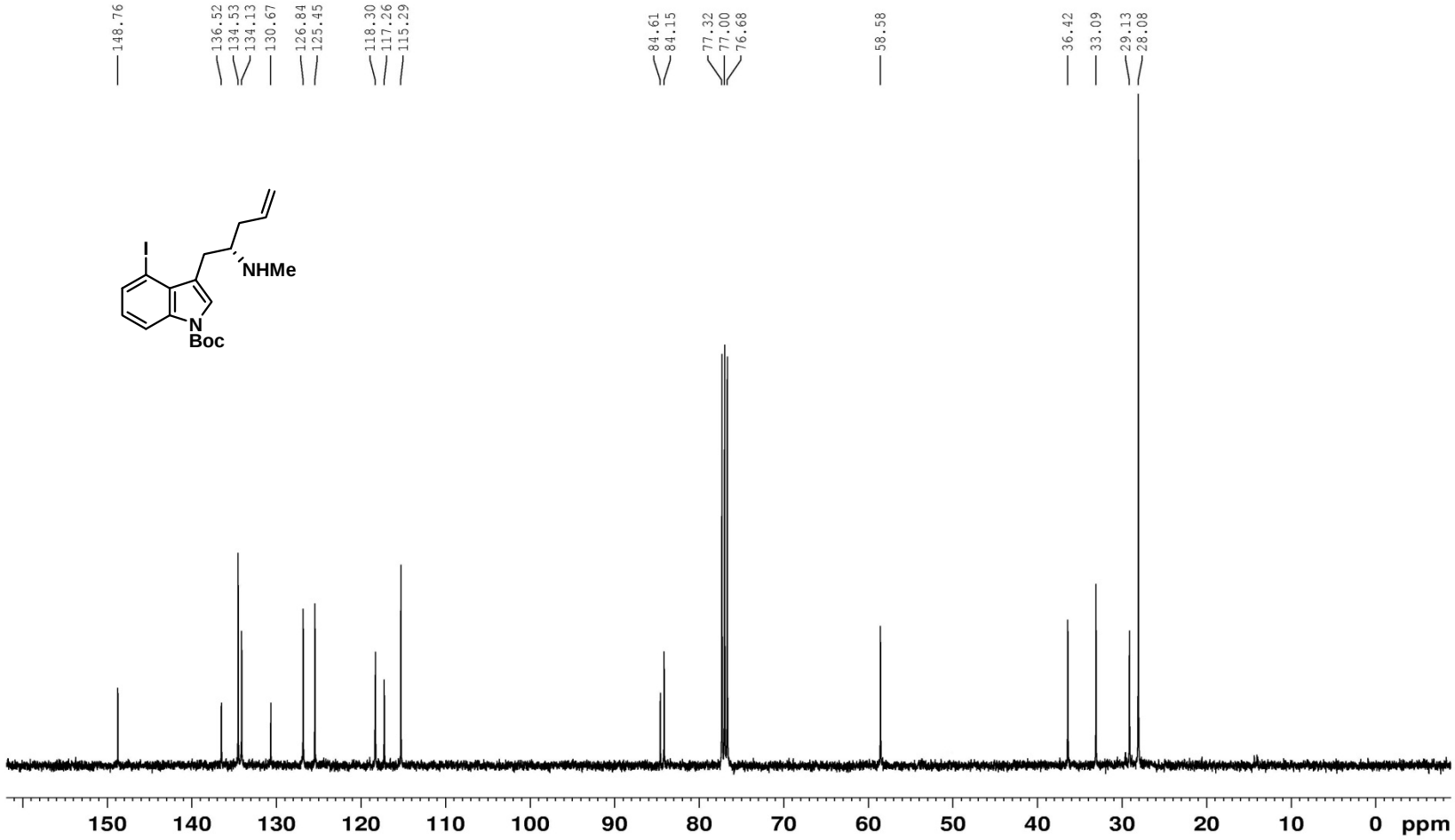
^{13}C-NMR of compound 10 (100 MHz, $CDCl_3$)



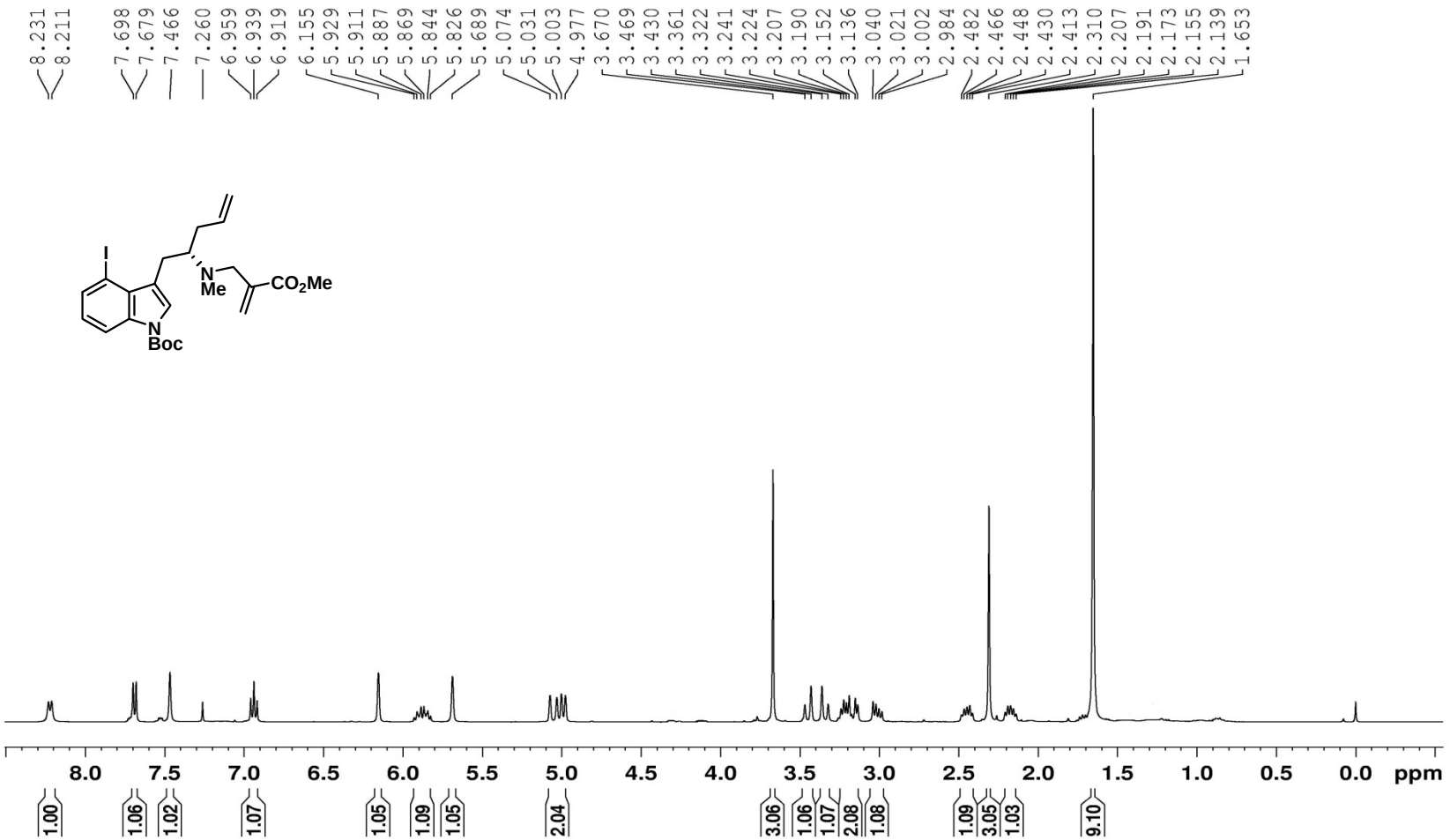
^{1}H-NMR of compound 14 (400 MHz, $CDCl_3$)



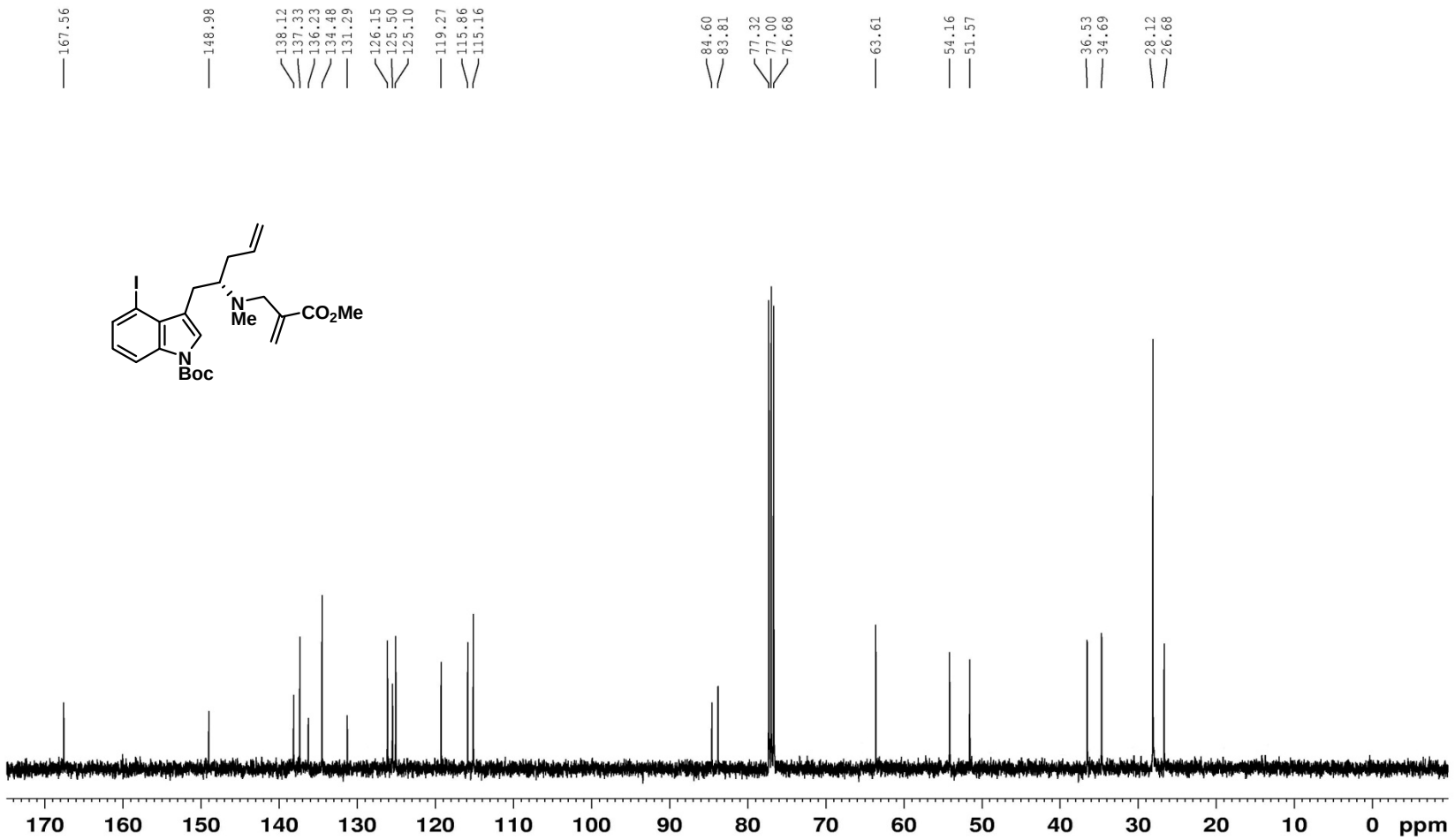
^{13}C-NMR of compound 14 (100 MHz, $CDCl_3$)



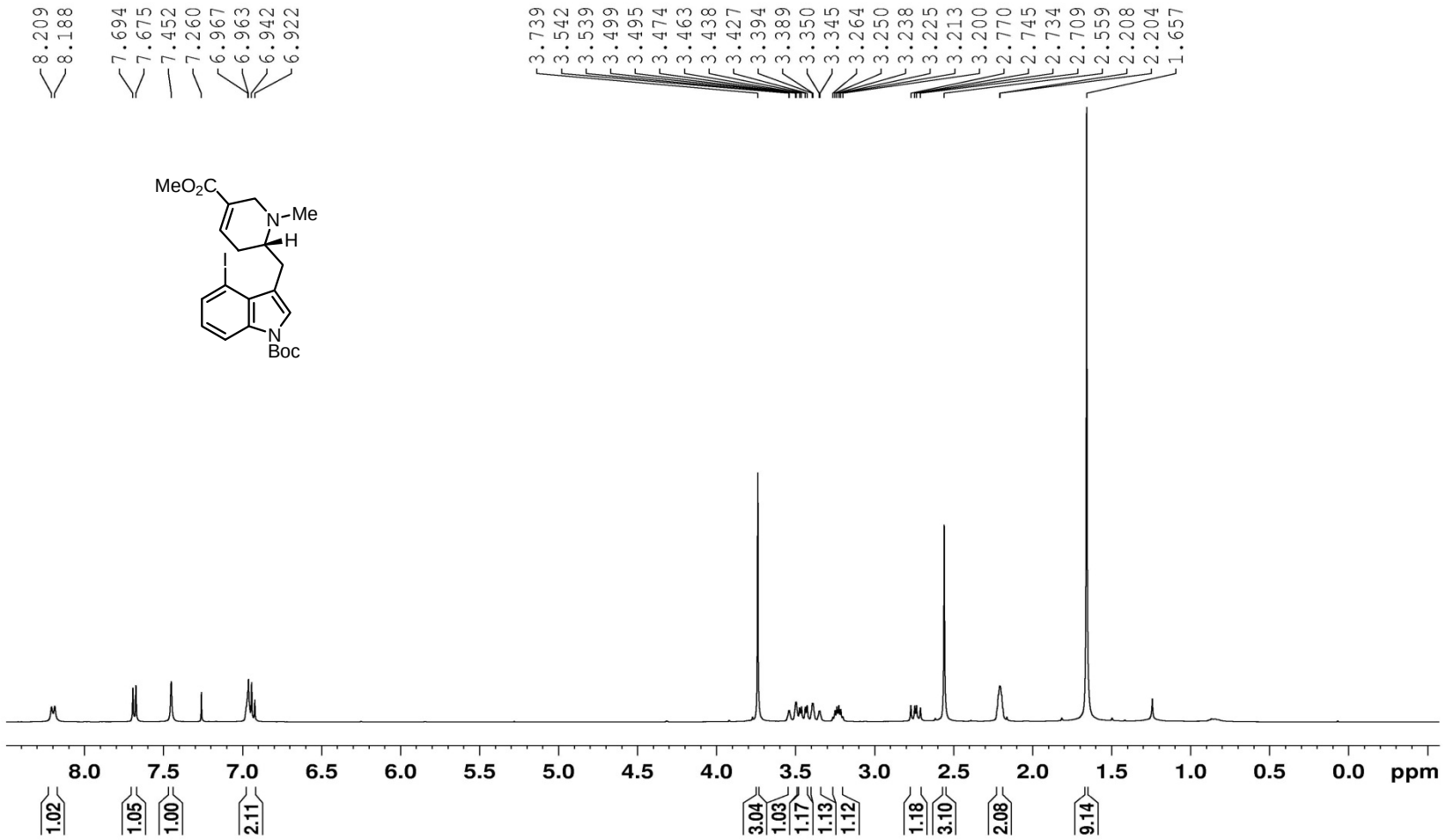
^{1}H-NMR of compound 4 (400 MHz, $CDCl_3$)



^{13}C-NMR of compound 4 (100 MHz, $CDCl_3$)



^{1}H-NMR of compound 3 (400 MHz, $CDCl_3$)



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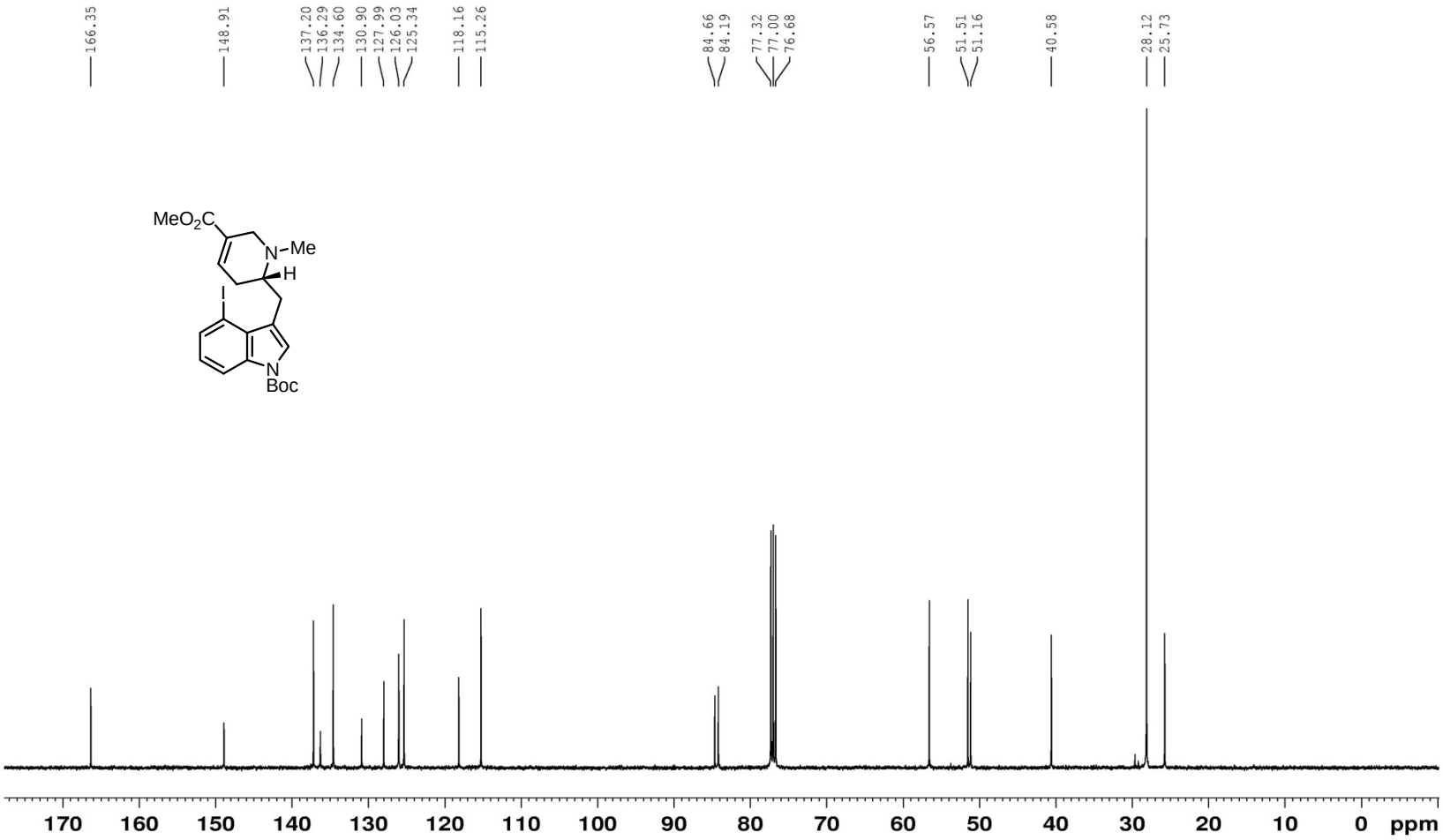
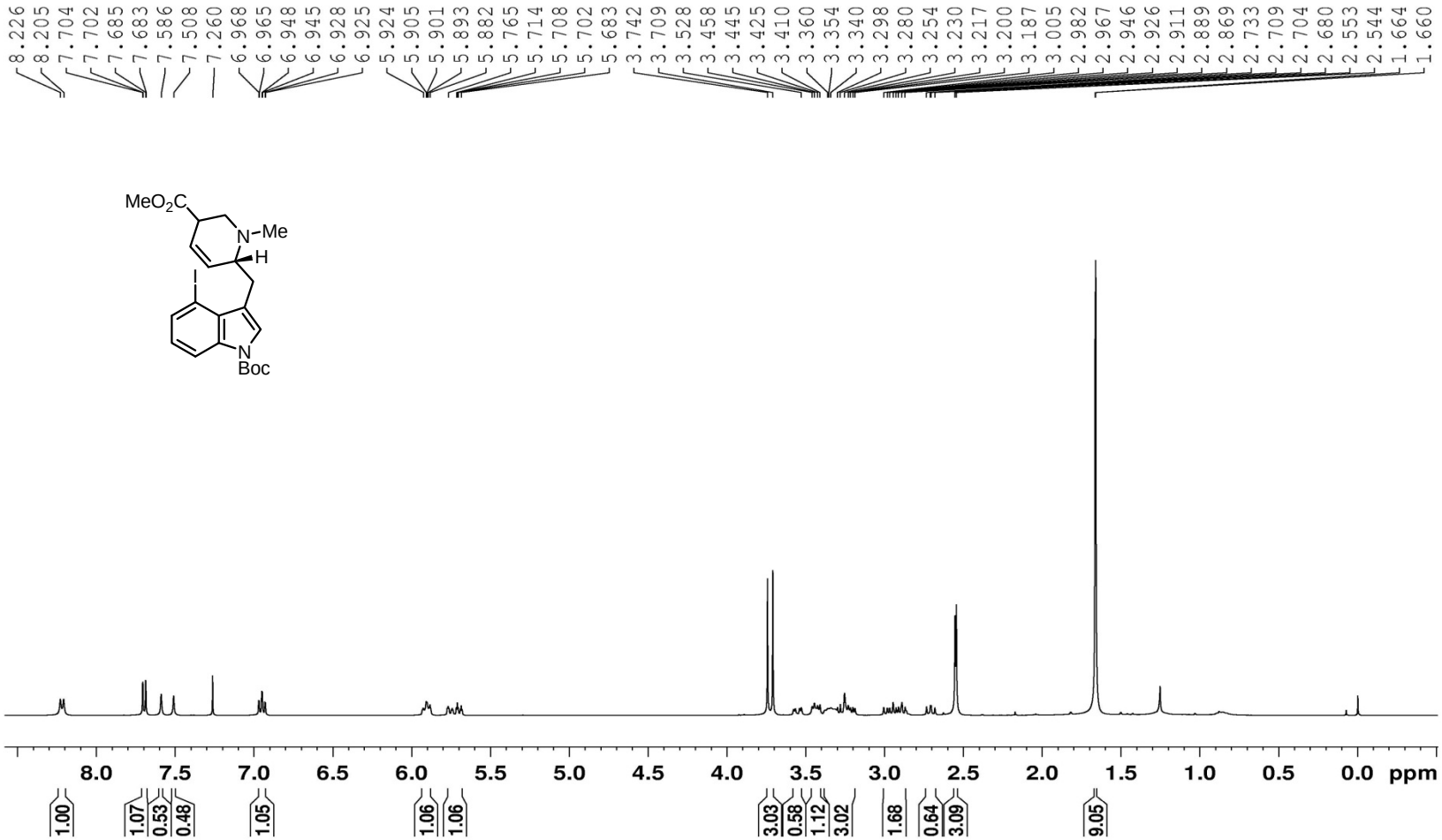
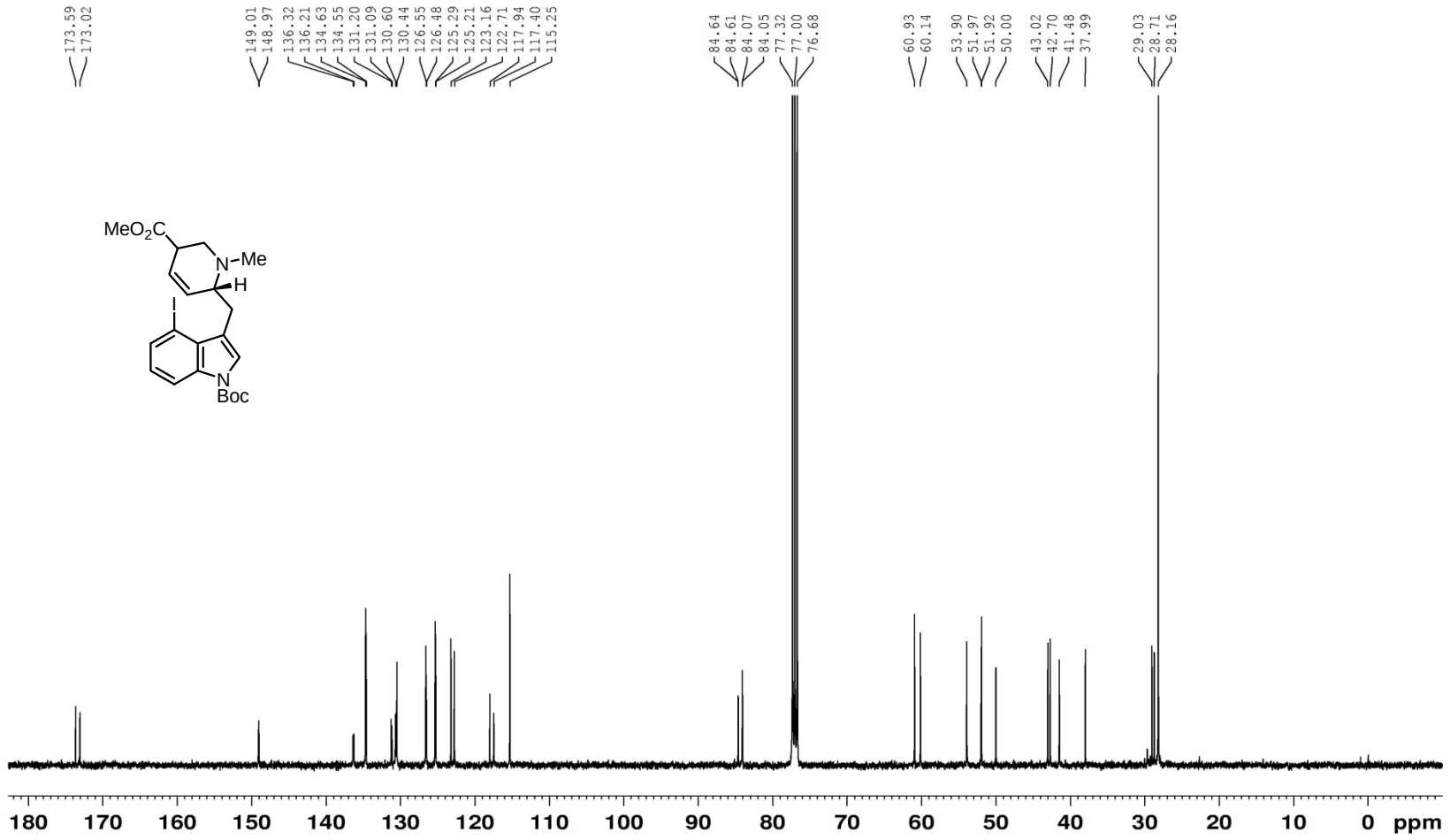


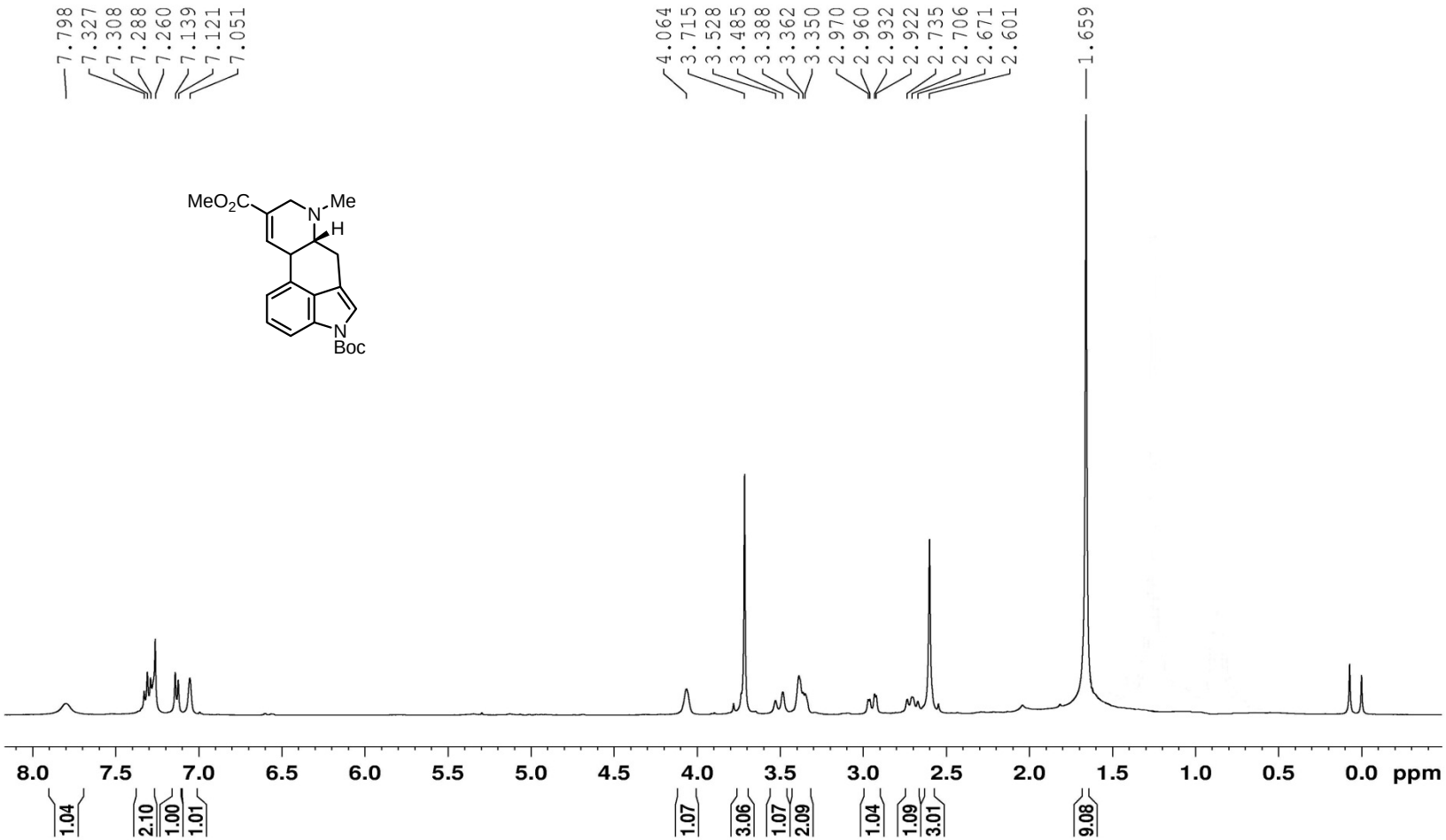
^{1}H-NMR of compound 2 (400 MHz, $CDCl_3$)



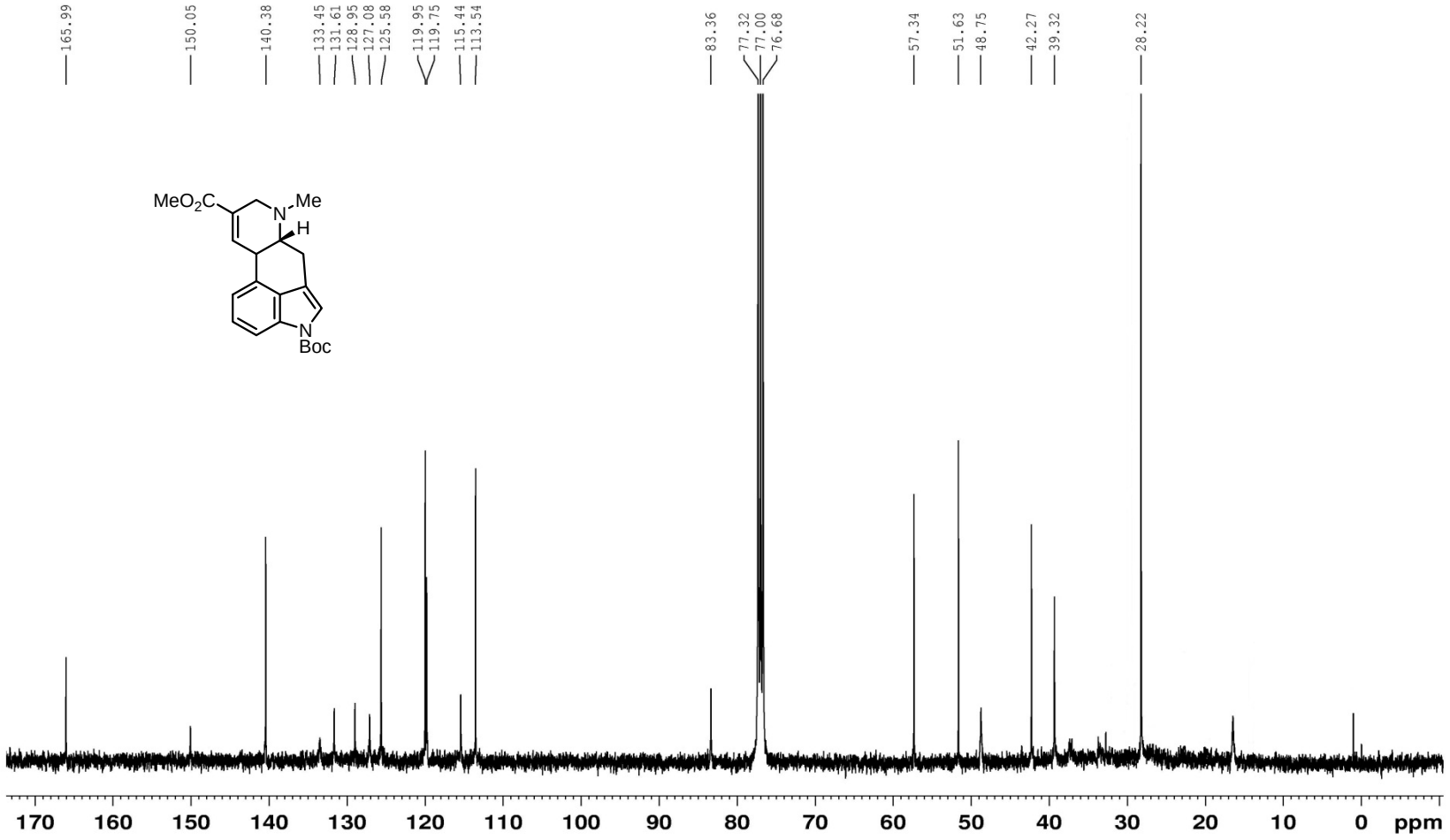
^{13}C-NMR of compound 2 (100 MHz, $CDCl_3$)



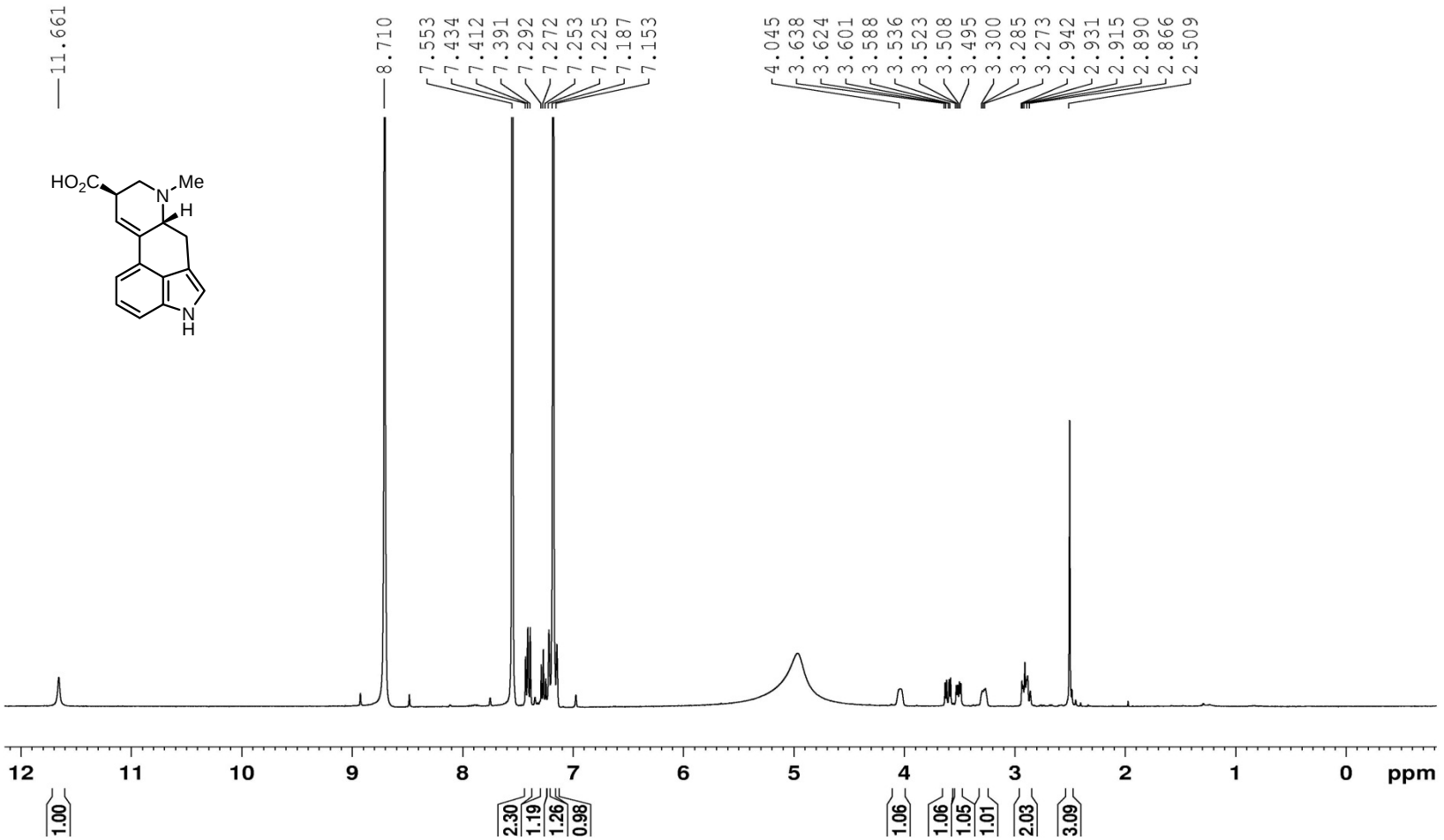
^{1}H-NMR of compound 11 (400 MHz, $CDCl_3$)



^{13}C-NMR of compound 11 (100 MHz, $CDCl_3$)



^{1}H-NMR of compound 1 (400 MHz, C_5D_5N)



^{13}C-NMR of compound 1 (100 MHz, C_5D_5N)